EFFECTS
OF
DIFFERENTIAL EXPERIENCE
ON
BRAIN AND BEHAVIOUR
IN THE RAT

G.J.M. VAN WOERDEN

Promotor: Prof. dr. J.M.H. Vossen

ISBN 90-9001216-8

EFFECTS
OF
DIFFERENTIAL EXPERIENCE
ON
BRAIN AND BEHAVIOUR
IN THE RAT

PROEFSCHRIFT

ter verkrijging van de graad van doctor in de sociale wetenschappen aan de Katholieke Universiteit te Nijmegen, op gezag van de Rector Magnificus Prof Dr. J H G I Giesbers volgens besluit van het College van Dekanen in het openbaar te verdedigen op donderdag 10 april 1986 des namiddags te 2 00 uur precies

door

Gerard Joseph Marie van Woerden

geboren te Nijmegen

Druk Dissertatiedrukkerij Wibro Helmond

This study was supported by a grant from the Psychonomy Foundation of the Dutch Organization for the Advancement of Pure Research (ZWO); Project no 15-25-02.

The investigations were carried out in the Psychological Laboratory, Department of Comparative and Physiological Psychology, University of Nijmegen, The Netherlands.

Aan mijn ouders
Aan Ied, Karel en Erik

DANKWOORD

Bij het verschijnen van dit proefschrift past een woord van dank aan de velen die - direkt dan wel indirekt - hun bijdrage hebben geleverd aan het tot stand komen van dit werk.
Allereerst gaan gevoelens van dankbaarheid uit naar mijn ouders. Hun belangstelling en interesse is altijd een inspirerende en motiverende bron geweest, en ik denk met dankbaarheid terug aan de volkomen natuurlijke 'enriched-environment' welke ik thuis heb mogen ervaren.
Voorts gaat mijn dank uit naar de medewerkers van de vakgroep vergelijkende en fysiologische psychologie. De samenwerking, het onderlinge overleg en de discussies in deze multidisciplinaire groep waren van het allerplezierigste soort. De daadwerkelijke bijstand van enkele leden van deze vakgroep vormde een belangrijke schakel bij het tot stand komen van dit werk. In het bijzonder denk ik hierbij aan M.Th.M. Jansen, die op soms buiten-normale werktijden en met een grote dosis frustratie tolerantie zijn medewerking gegeven heeft aan de uitvoering van enkele gedrags-metingen. Samen met J.C.M. Krijnen werd tevens voor een uitstekende verzorging van de proefdieren garant gestaan, waarvoor beiden mijn hartelijke dank.
Bij de opzet en pilot-studies van het onderzoek hebben G. Wittgen-Struik en M. Hovens, indertijd studenten, thans collega's, een enthousiaste bijdrage geleverd.
Zeker ook is een woord van dank op zijn plaats voor het begrip en bereidwillige instelling en behulpzaamheid van medewerkers van het Streekziekenhuis, in het bijzonder B. Hamers, R. Rothuis-ter Haar, Ph. Schoondermark en zeker ook collega G. Meyer, die de laatste maanden regelmatig een gedeelte van mijn taak in het ziekenhuis heeft overgenomen.
D. Veersema was zo vriendelijk behulpzaam te zijn bij het oplossen van print problemen. De figuren werden vervaardigd door F. Dexel.
De vertaling van dit proefschrift werd grotendeels verzorgd door Dr. J.P.M. Receveur terwijl Prof. Dr. G. Storms waardevolle adviezen en suggesties heeft gegeven, waarvoor ik beiden zeer erkentelijk ben.
Zonder in het bijzonder nog namen te noemen, wil ik verder allen, die op enigerlei wijze hebben bijgedragen aan het tot stand komen van dit proefschrift, hartelijk danken.

Tenslotte gaat veel dank uit naar Ied voor haar grote geduld, haar morele steun en het vele type-werk dat uit haar handen is gekomen. Samen met Karel en Erik heeft zij zich vaak afgevraagd wanneer het boekje nu eindelijk eens klaar zou zijn. Vandaag is het zover.

CONTENTS

CHAPTER 1

EFFECTS OF DIFFERENTIAL EXPERIENCE ON BRAIN AND BEHAVIOUR: GENERAL INTRODUCTION

CHAPTER 2

GENERAL PROCEDURE EMPLOYED IN ASSIGNING THE SUBJECTS TO THE VARIOUS CONDITIONS, AND DURING REARING

CHAPTER 3

EFFECTS OF DIFFERENTIAL EXPERIENCE (DUE TO REARING IN ENVIRONMENTS OF VARYING STIMULUS COMPLEXITIES) ON BODY WEIGHT AND REGIONAL BRAIN WEIGHTS

CHAPTER 6

EFFECTS OF DIFFERENTIAL EXPERIENCE IN ENRICHED (EC) AND IMPOVERISHED (IC) ENVIRONMENTS ON LATENT INHIBITION AND THE LEARNING OF A TWO-WAY ACTIVE AVOIDANCE RESPONSE IN THE SHUTTLE BOX

CHAPTER 7

PERSISTENCE OF BEHAVIOURAL EFFECTS, TEN MONTHS AFTER TERMINATION OF THE DIFFERENTIAL EXPERIENCE IN ENRICHED (EC) AND IMPOVERISHED (IC) ENVIRONMENTS

CHAPTER 1

EFFECTS OF DIFFERENTIAL EXPERIENCE ON BRAIN AND BEHAVIOUR: GENERAL INTRODUCTION

1.1. INTRODUCTION

Around 1780, the Italian anatomist Vincenzo Gaetano Malacarne wondered whether the training given to experimental animals had any influence upon their brains. Investigating the subject he used two dogs from the same litter and two birds from the same nest. One animal of each pair he extensively trained, whereas the other received no training at all. After a few years of this differential treatment he compared their brain weights. No differences were found (Rosenzweig et al., 1972b).
The idea that learning experiences might influence the structure and function of the brain persisted through the years. Thus, more recently, Hebb presented his hypothesis concerning permanent changes in the brain due to enriched experience, and suggested that the richness of the neural connections represents the neuroanatomical substratum of behaviour (Hebb, 1949).
This idea and the above-mentioned research method are found again in today's research concentrating on the effects of learning and external stimulation on the brain. Considering that the brain receives a continuous flow of information about the internal and external environment of the organism, one might wonder: does the brain function with a fixed structure when it receives and processes all this stimulation, or, alternatively, does the brain change due to this stimulation, and if so, does this change in its turn influence later behaviour?

Only in recent decades have clear indications been found that environmental variables, such as light and acoustic stimuli, as well as learning and memory processes may induce chemical and anatomical changes in the brain. Plasticity of the brain as induced by the environment is investigated nowadays mainly by manipulating either an aspect of the sensory environment, e.g. differentiation in the visual stimulation, or the entire sensory environment of the subjects. Thus, it has been demonstrated that monocular as well as binocular visual deprivation induces a decrease in the density of visual cortical synapses and dendritic spines. Physiological, anatomical and behavioural studies (a.o. Hubel and Wiesel, 1970) all indicate that the neural network of the visual system is very sensitive to deprivation effects (Cragg, 1969; Ruiz-Marcos and Valverde, 1969; Fifkova, 1970a, b and c; Cragg, 1975), particularly so during a critical period in the development (Dews and Wiesel, 1970; Hubel and Wiesel, 1970), but also during adult life in a completely matured central nervous system (Fifkova, 1970a; Creutzfeldt and Heggelund, 1975).

Various levels of general sensory deprivation and stimulation have a clear effect on the brain's structure also. This became apparent particularly in the research of a group of investigators at the University of California in Berkeley, California, U.S.A.
Around 1960 this group composed of researchers from various scientific disciplines started an extensive research programme, studying, in rats, the influence of prolonged exposure to environments of varying stimulus complexity on various chemical and anatomical variables of the brain. This research was an extension of earlier investigations by the same scientists (Bennett, Diamond, Krech, Rosenzweig and coworkers). In 1954 and 1956 Krech et al. reported that rats that differed in hypothesis-behaviour in a maze (developed by Krechevsky), also differed in cortical Acetylcholinesterase (AChE) activity. Subjects that had a preference for spatial hypotheses appeared to have a higher specific AChE activity in the visual as well as the somesthetic cortex than subjects which preferred visual hypotheses. Moreover, rats from a strain that had been genetically selected by Tryon (1940) on the basis of good performance in a maze, appeared to have a higher concentration of acetylcholine and more AChE per mg wet brain tissue in their brains than rats from another strain, genetically selected by Tryon on the basis of bad performance in a maze (Rosenzweig, Krech and Bennett, 1960). The issue was whether these biochemical variables that appeared to be correlated with learning performance in various mazes, did possess enough plasticity to render them modifiable by learning experiences. Initially, learning experiences were defined in terms of formal training as well as in terms of prolonged exposure to environments of diverse stimulus complexities. In the course of the experiments conducted after 1960, the researchers found to their surprise that living in environments of different simulus complexity alone, that is, even without any explicit formal training, was sufficient to induce clear and consistent effects on brain anatomy as well as brain chemistry.
These neurochemical and neuroanatomical changes, brought about by staying in environments of differing stimulus complexities in their turn appear to have consequences in behaviour, e.g. in learning behaviour. Environmental and learning experiences in this way - indirectly - influence later behaviour. Both data: the changes in nuerochemical, neuroanatomical and neurophysiological variables and the changes in certain aspects of behaviour offer a good opportunity to investigate the brain-behaviour relation.
The thus created - indirect - effects of differential experience on behavioural variables have been but little investigated by the Berkeley group. The main purpose of this dissertation is to gain more insight into the effects of staying in environments of varying stimulus complexities on behavioural variables.

Bennett, Diamond, Krech and Rosenzweig employed three different environmental conditions in their studies of the effects of environmental complexity on the brain.

The first condition was presented by the standard laboratory condition (SC, standard condition), consisting of a cage of 32*20*20 cms, in wich three rats were housed simultaneously. The second condition was stimulus-enriched (EC, enriched condition). In this condition, 10 - 12 rats were housed together in a large cage (70*70*46 cms) in wich various objects (ladders, wooden blocks etcetera) were placed. These objects were changed daily. About six out of a supply of 30 were placed in the cage each day. The objects used have been described and illustrated in an article by Rosenzweig and Bennett (1969). In some of the earlier experiments of the Berkeley group (before 1968) the animals were given the opportunity to explore together a Hebb-Williams maze during 30 minutes a day, with the positions of the partitions in the maze changed each day. Besides, these animals received training in the Lasley-III maze, the Dashiell maze, and the Multiple Discrimination Box (KMDB) developed by Krechevsky. This formal training programme as well as the opportunity to explore the Hebb-Williams maze, were dropped from the programme from 1968 onwards, because they did not further contribute to the effects of prolonged exposure to the enriched environment.
The third condition, finally, consisted of a stimulus-impoverished condition (IC, impoverished condition). The animals of this condition were housed individually in the same cages as the standard condition animals. Initially, these cages had opaque walls to prevent the animals seeing each other. Later it appeared that animals, housed individually in transparent cages in an illuminated and busy laboratory room, did not differ from the original extra-deprived animals with respect to the brain variables under study.

Housing rats several days in these environments of varying stimulus complexities (also called: differential experience) appears to influence a large number of neurochemical, neurophysiological and neuroanatomical variables.

1.2. EFFECTS ON BRAIN CHEMISTRY

The Berkeley researchers reported that a stay of 30 to 80 days in the various environments has an effect on the AChE activity in the brains of the animals. The total AChE activity found in the occipital cortex and in the entire cortex is increased in EC subjects, compared with IC subjects (Bennett et al., 1964, 1970; Rosenzweig, 1971; Rosenzweig and Bennett, 1978). This increase in AChE activity found in EC animals is less than the increase also found in the weight of the cortex; thus, the AChE activity per mg brain tissue is less in EC animals than it is in IC animals.
These AChE effects have been replicated in several laboratories, in rats as well as mice. Moreover, the effects on many other neurochemical variables have been studied; for example, S-100 protein (Hyden and Roennbach, 1979); the in vitro RNA-synthesis by brain chromatin (Uphouse and Moore,

1978; Uphouse, 1978); RNA diversity (Grouse et al., 1978); the incorporation of aminoacids into protein (Hyden and Roennbach, 1978). For an extensive review of the results, the reader is referred to the articles of Rosenzweig, Bennett and Diamond (1972b), DeFeudis (1975, 1979), Bennett (1976), Rosenzweig and Bennett (1978) and Walsh (1980a and b).
Generally spoken, the effects on the various neurochemical variables tend to regional as well as temporal specificity; the largest effects are often found in the occipital cortex. As Walsh remarks:

> "greater complexity of the sensory environment results in increased total cholinesterase and acetylcholinesterase enzyme activity, while other neurotransmitter-related substances, the catecholamines, show more variable responses" (Walsh, 1980a, page 77).

1.3. EFFECTS ON BRAIN PHYSIOLOGY

Differential experience not only influence neurochemical variables, but neurophysiological variables are affected as well. Research in this area was conducted, among others, by Melzack (1969). In his investigations he used dogs reared in isolation in a bare environment and dogs reared in normal groups and a normal environment. He compared the EEG's of both groups. After placing the animals individually in closed boxes, he found that when subjects were allowed to see through an opening in the box towards another environment, the reticular and cortical EEG's of animals reared in isolation showed a remarkable change from lower to higher frequencies (indicating high levels of EEG-arousal). Changing back to lower frequencies occurred only after closing off the view of the novel environment. The EEG's of dogs reared normally showed only short lasting changes to higher frequencies in comparable situations, and these changes were never as large as those found in the isolated dogs. Moreover, the EEG patterns of the normal dogs returned to the former low frequency before the view of the novel environment was closed off (Melzack, 1969). Melzack also noted much larger variability in the EEG's of the dogs reared in isolation, compared with the more stable, homogeneous records of the dogs reared normally. He concluded:

> "Processing of sensory information in restricted dogs, during the high arousal states produced by an unfamiliar environment, differs from that in normal dogs showing more moderate levels of arousal" (Melzack, 1969, page 725).

Another effect of differential rearing on the processing of sensory information has recently been discovered in a study of evoked cortical potentials of EC and IC rats. After repeated presentations of a tactile stimulus, the evoked potentials of the EC animals showed an amplitudo decrease, whereas the potentials of the IC animals did not change. However, when the experiment was repeated one hour later,

both groups of subjects showed a decrease in amplitude (Leah, Allardyce and Cummins, 1985).
The occurrence of brain effects due to differential experience is considered to be caused to a large part by differences in learning experience and memory formation. Animals living in an enriched environment are occupied much more than animals in an impoverished situation, with the processing and storage of information (Rosenzweig and Bennett, 1977). One theory suggests that REM sleep plays an important role in the processing of learning experiences as well as in the processing, maintenance and storage of long-term memory (e.g. Gutwein and Fishbein, 1980a and b). One might expect, then, that animals from an enriched environment show more REM sleep than animals from impoverished conditions. Research into the possible effects of differential experience on REM-sleep has shown that exposure to enriched environments results in an increase of Slow Wave Sleep (SWS) as well as paradoxical sleep (PS or REM sleep; Tagney, 1973; Gutwein and Fishbein 1980a en b; Kiyono et al., 1981; Mirmiran et al., 1982). Gutwein and Fishbein also noted an increase in the percentages PS of total sleep in EC animals. Recent investigations have demonstrated that also in older rats exposure to an enriched environment leads to an increase in REM sleep (Van Gool and Mirmiran, 1984).

1.4. EFFECTS ON BRAIN ANATOMY

Besides the effects on neurochemical and neurophysiological variables, effects of differential experience on neuroanatomical variables have been found also.
A much published finding is that subjects which remain in an enriched environment for some time, develop a heavier cerebral cortex in comparison with animals that stay in an impoverished environment for some time (Diamond, 1976). The proportionally largest weight differences are always found in the occipital region of the cortex. The subcortex of EC and IC animals apparently does not show clear differences in weight. Hence, EC animals almost always show a higher cortex/rest of brain weight ratio.
Besides this differential experience effect on the weight of parts of the cortex, effects upon a large number of other variables have been found also, particularly so in the occipital cortex. For example, effects have been found on the neuronal perikaryon and nuclear size, the extensiveness of higher-order dendritic branching, the amount of dendritic spines, the size of postsynaptic thickening and the number of neuroglial cells (e.g. Diamond et al., 1964, 1966, 1967; Globus et al., 1973; Uylings et al., 1978).
Besides the occipital region the hippocampus has been investigated rather extensively as to possible effects due to differential experience; this research was directed mainly to the gyrus dentatus and studied size of neurons, variability in nuclear size, dendritic ramifications and number of neuroglial cells (e.g. Walsh, Budtz Olsen, Penny and Cummins, 1969; Fiala, Joyce and Greenough, 1978; Walsh

and Cummins, 1979). The effects found here are not as clear as those found in the occipital cortex and are easily masked by large interindividual differences. Therefore, these hippocampal effects could not always be replicated successfully (Diamond, 1976).
For an extensive review of the neuroanatomical effects, the following reviews are recommended: Bekoff and Fox (1972), Diamond (1976), Rosenzweig and Bennett (1976, 1978), Jones and Smith (1980), Walsh (1980b and 1981a).

1.5. EFFECTS ON THE RESULTS OF MANIPULATIONS OF BRAIN FUNCTION

The above-mentioned results of neurobiochemical, neurophysiological and neuroanatomical research make clear that the nature of the environment an organism lives in influences the structure of its brain. This, then, is a manifestation of the structural plasticity of the brain. The brain does not have a completely fixed structure. On the contrary, it develops from its first beginning with a building scheme which contains the experience of the species. This building scheme provides the basis of structures but also the capacity for variability: the building scheme is not yet finished as it were, but is completed, changed, adapted by environmental stimuli. Bekoff and Fox put it this way: the postnatal ontogeny is environment-expectant and -dependent. The brain develops in the expectancy of a certain environment and may correct itself in consequence of the real situation (Bekoff and Fox, 1972).
The role played by the environment and differential experience in general with respect to structure and functioning of brain and behaviour, is illustrated by the fact that environmental influences play an important part in
- the behavioural effects due to brain damage (reviews: Donovick et al., 1979; Stein et al., 1983; Walsh, 1981b).
- the rate of recovery after induced cerebral damage (influence is exerted by the pre-surgery environment (Donovick et al., 1973; Goodlett et al., 1982) as well as the post-surgery environment (Eclander and Karli, 1980; Goodlett et al., 1982; Will et al., 1976, 1977)).
- the effects of psychopharmaca on behaviour (e.g. Coyle and Singer, 1975).
- behavioural effects of ECS administration (Calhoun et al., 1975).

For example, it appears that in animals exposure to an enriched environment positively affects the seriousness of behavioural defects as well as the recovery process after cerebral damage to the septum (Donovick et al., 1979; Engellemer et al., 1982), the visual cortex (Schwartz, 1964; Will et al., 1976, 1977), and the sensomotor cortex (Held et al., 1985; Whishaw et al., 1984). Hence, when studying the influence of psychopharmaca and the effects of brain lesions as well as the recovery processes afterwards, it is important to take into account the environmental conditions of the subjects, that is to say, the environment the animal

was in previous to the treatment concerned, as well as the environment it was in after this treatment.
It now may be clear that "environmental therapy" might have some importance in aiding recovery from brain damage and the resulting behavioural dysfunctions.
The Berkeley group suggest that cerebral effects due to differential experience represent mainly an integration or cummulation of a continuing series of pulses of biochemical synthesis that occur as consequences of learning events (Rosenzweig et al., 1972b). Walsh summarizes:

> "It is probably simplistic to think of neuronal interconnections in adult brain as fixed and static. Probably a more adequate picture is provided by a dynamic model in wich axonal, dendritic, and synaptic growth is in constant dynamic flux. The net result would approximate homeostasis, unless sensory input or other modifying factors resulted in a shift towards another homeostatic balance point" (Walsh, 1981a, page 48).

1.6. CAUSAL FACTORS

Of course, scientists addressed themselves to the issue of what factors in the various environmental conditions are fundamental in causing the above-mentioned effects upon the brain. Another question asked was whether the effects could be obtained only during the development to adulthood, and if so, whether critical periods could be pointed at, or whether the effects could also be demonstrated in adult, fully mature animals. Both questions evoked a large number of studies that produced the following, summarized, pattern of results:

- Effects of enrichment/impoverishment on the brain are found in young as well as older, adult rats (Rosenzweig et al., 1964). In younger rats the effects are comparatively larger (Riege, 1971; Diamond, Johnson and Ingham, 1975; Warren, Zerwich and Anthony, 1982).
- Effects of differential experience on brain values cannot be attributed to a difference in the rate of maturing. In their review Rosenzweig and Bennett concluded that "a number of anatomical and biological measures are differentially modified by maturation and by enriched environments, so we conclude that EC/IC differences cannot be attributed to maturational effects" (Rosenzweig and Bennett, 1976, page 190).
- In young rats, staying in enriched and impoverished environments during three days immediately after weaning is sufficient to demonstrate brain effects (Zolman and Morimoto, 1965; Rosenzweig and Bennett, 1978). After being kept in the various environments for 7, 14, 30 and 80 days, these brain effects are still present. The effects upon cortex weight is most pronounced after a period of 25 to 55 days in those environments (Bennett et al., 1970).
- Rats, reared in standard condition cages up to the age of one year and subsequently, at an adult, mature age, placed in enriched and impoverished conditions for 30, 60 or 90 days, developed EC/IC effects similar to those found in

young, still developing rats (Riege, 1971). Comparison with the standard condition (SC) reveals that the effect upon brain weight is caused mainly by the EC condition, in older as well as younger rats (Rosenzweig et al., 1964; Riege, 1971). Obviously, the brain of adult rats retains a clear plasticity, even after termination of the neuronal growth phase (Rosenzweig, 1971). The phenomenon that - in adult animals also - the nervous system is capable to undergo longlasting and specific changes as a consequence of experience, is termed plasticity. Thus, plasticity is defined as comparatively longlasting and specific changes in the composition of the nervous system in relation with experience and physiological stimulation (Horn, 1973).

- Staying in the various environments for two hours per day is sufficient to evoke the usual EC/IC effects upon brain weight (Rosenzweig et al., 1968). These effects were not obtained when the rats were individually exposed to an enriched environment during two hours a day (Bennett et al., 1964). However, when the activity of the animals staying in the enriched environment individually was increased by either the administration of methamphetamine or the location of the two hours exposure to the enriched condition into the dark period of the light/dark cycle of the animal, the previously mentioned EC/IC effects reappeared (Rosenzweig et al., 1968; Rosenzweig and Bennett, 1972).
- The effects on brain weight cannot be reduced to effects upon body weight. After a period of 24 hours a day in an enriched environment the changes in body weight and brain weight are in reversed directions; after a period of two hours per day only in the enriched environment no effect upon body weight is found, whereas the effect upon brain weight is as large as the effect obtained after a stay of 24 hours a day in that environment (Rosenzweig et al., 1968; Rosenzweig and Bennett, 1972).
- The opportunity for higher daily locomotor activity in the EC condition is in itself not sufficient to produce the brain effects. Krech et al. (1960) and Zolman and Morimoto (1965) studied the effect of a respectively 14 and 30 days period of daily locomotor activity for a few hours per day upon brain weight: no effects were found. Rosenzweig (1966) compared an EC group with a "normal" IC group as well as with an IC group that ran in a running wheel during two hours a day. The IC groups did not differ, but both differed from the EC group to the same degree. Huntley and Newton (1972) did a similar experiment. However, they found that the IC group which had this locomotor activity scored between the EC group and the normal IC group with respect to brain weight and did not differ from either.
- From experiments by Bennett et al. (1964), Rosenzweig (1966), Rosenzweig and Bennett (1968) and Riege and Morimoto (1970) it may be concluded that daily handling does not influence the development of the EC/IC differences.
- Stress does not appear to play a part in the development of the EC/IC effects either. Stress has hardly any

influence upon brain weight, though it has upon the weight of the adrenal glands (Riege and Morimoto, 1970). Stress versus no-stress does not produce effects comparable with those caused by rearing in enriched and impoverished conditions (Rosenzweig and Bennett, 1976).

- Hormonal regulation and excretion by the hypophysis are not necessary to enable the development of EC/IC effects upon brain weight (Rosenzweig et al., 1972a). In a review of the influence of stress and hormonal regulation Uphouse (1980) emphasizes that these variables in interaction with many other factors of a physiological nature, still might contribute to the development of the EC/IC differences.
- Although the largest EC/IC effects are found in the occipital cortex, it is remarkable that visual stimulation is not a necessary condition for the development of these effects. Blindness and growing up in total darkness in itself have an effect upon the weight of the occipital cortex and upon the development of dendritic spines in that area (Valverde, 1971), but do not influence the development of EC/IC effects on the occipital cortex (Krech et al., 1963; Rosenzweig et al., 1969).
- What does seem to be of paramount importance for the development of EC/IC effects, is the opportunity that EC animals have for active - interactive - tactile contact with peers and objects. This opportunity appears to be a necessary condition: when animals were reared in isolation in IC cages that were placed in EC cages, the full development of the differences in brain variables between these IC animals and EC subjects was not prevented (Ferchmin and Bennett, 1975).
- Whether the fact that the animals of the enriched condition live in a large social group is sufficient in itself to induce the various effects, is not clear. Initially, the Berkeley group did not find significant differences between rats reared in a bare EC cage and IC rats (Rosenzweig and Bennett, 1972). In more recent papers, however, it is reported that social stimulation still might play a role in the development of differential experience effects on brain variables (Rosenzweig et al., 1978).

1.7. EFFECTS ON BEHAVIOUR

While studying the effects of differential experience, the Berkeley group also payed attention to behavioural effects. They reported that EC rats made less errors than IC rats in a Lashley-III maze (Rosenzweig, 1971). They also found that after a period of 30 days in the various environments, EC and IC rats did not differ as to the learning of a single light-dark discrimination, whereas in the subsequent reversal tasks IC rats performed less well than EC rats (Krech et al., 1962). The latter was found only if the isolation of the IC animals started immediately after weaning.

Following those positive results obtained by Bennett, Diamond, Krech and Rosenzweig with respect to the

neurochemical and neuroanatomical variables investigated, a number of scientists from other laboratories carried out experiments that studied the aspects of exposure to enriched and impoverished environments on a large variety of behaviours in rats and mice. To mention a few: complex maze learning (Hebb-Williams maze, Lashley-III maze, Dashiell checkerboard maze), exploratory behaviour, locomotor activity, avoidance behaviour, success in a food competition test, hoarding behaviour, emotionality, etcetera (for reviews, see: Meyers, 1971; Bennett et al, 1970; Rosenzweig, 1971; Greenough, 1976; Rosenzweig and Bennett, 1977).
One of the most consistent results is that EC animals learn complex mazes faster than IC animals do. However, the fact that sometimes rats, sometimes mice were used as subjects, the large variation in the types of enriched and impoverished environments in which the animals were placed, and the diversity in the techniques used to measure the behaviours, render a comparison and evaluation of the results quite difficult.

1.8. HYPOTHESIS

With respect to the question in which way behaviour is influenced -indirectly- by rearing in environments with varying stimulus complexities, the effects on AChE activity might represent a cue. AChE plays an important role in the cholinergic synaptic transmission; therefore, it is conceivable that through their different experiences EC and IC animals have developed cholinergic systems that function differently.
An indication for this hypothesis may be found in research focusing on influencing the cholinergic system in EC and IC animals (Greenough et al., 1973). This research revealed that EC and IC rats react differently upon the administration of the cholinesterase physostigmine. Greenough et al. first trained EC and IC animals in a Lashley-III maze. Immediately after training the animals were assigned to various groups and injected with either saline or physostigmine. Several doses were used. The effect of this post trial administration of physostigmine, in a dose ranging from 0.5 to 1.5 mg/kg, was a facilitation of relearning after a 24-hours interval in the EC rats; this facilitation effect showed a U-shaped relationship with dose-range. No facilitation effect was found in the IC group. Thus, differences were found with respect to the influence of physostigmine in EC and IC animals respectively, which points to a difference in the functioning of the cholinergic system of both groups.

What role, then, does the cholinerg system play in behaviour? In recent years this issue has evoked a large mass of research (Carlton, 1963, 1968, 1969; Deutsch, 1966, 1969, 1971; Warburton and Brown, 1971; Warburton, 1972, 1977; Warburton and Wesnes, 1984). In these studies the cholinergic synaptic transmission has been manipulated by administration of either anticholinergics such as

scopolamine and atropine, or anticholinesterases such as physostigmine, and the effects of the thus altered cholinergic activity on a large variety of behaviours have been studied. Carlton, Deutsch and Warburton, however, do not arrive at the same conclusion with respect to the influence of the cholinergic system on behaviour.

On the basis of his results Carlton formulates the hypothesis that within the central nervous system at least two interacting systems exist, which can be chemically and anatomically differentiated and which both influence behaviour: an adrenergic and a cholinergic system. The adrenergic system mediates diffuse behavioural activation: it controls the likelihoud with which the various responses at the animal's disposal will occur; it is -as it where- the motor of behaviour. The cholinergic system, on the other hand, directs behaviour towards effective response patterns by inhibiting nonrewarded, irrelevant responses. Carlton puts it as follows:

> "It thus appeared that some cholinergic system antagonized the diffuse effects of activation and that this antagonism, first, might provide a basis for "selection" of the effects of activation and, second, was related to the extent that certain responses were *correlated with nonreinforcement*. Thus, level of activation could be viewed as controlling the tendency for all responses to occur, whereas an inhibitory cholinergic system would act to antagonize this action on nonreinforced responses. The net result of this interaction would be that changes in activation would result in changes in the likelihood of occurrence of only a few responses, those that were reinforced" (Carlton, 1963, pag.27; author's italics).

The adrenergic system was assumed to act mainly through the reticular formation, the cholinergic system through septum and hippocampus. Carlton's ideas on inhibition are closely connected with the traditional use of the concept of inhibition, which denotes a decrease in the functioning of one system through activation of another.

With respect to the function of the cholinergic system Deutsch formulated another hypothesis; according to him the cholinergic system plays a role in memory processes. More specifically, it was thought to play a part in the transition of short term memory (STM) to long term memory (LTM; Deutsch, 1971). However, research by Brown and Warburton (1971) and Cheal (1981) demonstrated that scopolamine rather influences attention and stimulus sensitivity and only indirectly, through these, affects memory processes.

In an extensive review Warburton (1977) described the phenomenon of behavioural inhibition and the role of the cholinergic system and possible other systems therein. Warburton agrees with Carlton that the cholinergic system plays a part in the inhibition of behaviour. Behavioural inhibition may result from three distinguishable processes: stimulus selection, decrease of activation and response inhibition. Warburton's conclusion as to which process mediates behavioural inhibition by the cholinergic system

differs from Carlton's suggestion. After analysing a large number of experimental data, including Carlton's, Warburton shows that the inhibitory cholinergic system exerts its influence upon stimulus input rather than response output. It plays a part in filtrating stimuli that are not relevant for the organism. Thus, with respect to the regulation of behaviour the cholinergic system is important for the inhibition of behaviour by playing a part in stimulus selection; this way it modifies behavioural inhibition (Warburton, 1972, 1977; Warburton and Wesnes, 1984). Warburton arrives at this conclusion after a thorough study of Carlton's and other scientists' results as well as his own research, all of which focus on the influence of cholinergic, adrenergic and serotonergic systems upon behaviour, behavioural inhibition in particular. These studies were concerned mainly with habituation, extinction, discrimination learning and response suppression by aversive stimuli (Warburton, 1977). Warburton's conclusions can be summarized as follows: 'decrements in responding that have been interpreted as instances of behavioural inhibition could have been the result of changes in three systems: either stimulus selection or activation or response inhibition.

A response inhibition mechanism would refer to some systems which reduced or abolished the response output. This behavioural inhibition pathway is considered to have serotonine as its transmitter. It has its origin in the tegmental region and projects to the septal area as well.

An activation mechanism is one that energizes the response. This system is considered to be a dopamine pathway that passes ventrally through the hypothalamus from the interpeduncular nucleus to the nucleus accumbens septi. The system appears to be mediating behavioural activation.

The stimulus selection system refers to a system wich selects from the mass stimuli bombarding the sensory receptors. This system is considered to be a cholinergic pathway that ascends from the reticular formation to the cortex. The system seems to be mediating stimulus selection' (Warburton, 1977, pages 421-422).

The stimulus selection process filtrates irrelevant aspects of the environment by inhibiting the input that arrives through the primary sensory pathways. In animals that have a badly functioning cholinergic system the total stimulus intensity is different, probably larger than in normal animals, in the sense that the former have a lowered stimulus sensitivity threshold for all stimuli, including the irrelevant. Hence, they cannot easily distinguish figure and background, or, in other words, they cannot form a proper gestalt (Vossen, 1968; Warburton, 1972). It is evident that -in the end- this process is of the utmost importance for adaptive behaviour, learning and memory also.

Let us now consider the effects of differential experience on brain AChE and the theory on the influence of the cholinergic system upon behaviour. The above-summarized data support the assumption that exposure to either an enriched or an impoverished environment might affect the efficiency of stimulus selection. The goal of the research reported in

this dissertation may now be formulated more explicitly: this research aims to investigate whether, and if so to what degree, living in environments of different stimulus complexities affects the efficiency of stimulus selection, particularly the filtration of irrelevant stimuli. To this end a number of different test situations have been employed.

With respect to the problem in which way behaviour is affected by the animals being reared in environments of different stimulus complexities, a number of hypotheses have been proposed in recent years, which are based on the behavioural differences reported. We will discuss these hypotheses and compare them with our own.
The first hypothesis proposed is that EC and IC animals differ from each other as to level and duration of arousal. Walsh and Cummins (1975) arrive at this conclusion after observing that rats staying in enriched environments show more arousal than rats in impoverished environments. They conclude that the animals are continuously exposed to arousal-inducing situations (e.g. the daily changing of stimulus objects and social interaction) and learn to more or less habituate. Consequently, in later unfamiliar situations, the EC rats show arousal reactions that are weaker and decrease faster than those of the IC rats. Thus, the later behaviour of EC and IC rats differs in intensity and duration of the arousal induced by novel situations. With respect to this theory the following remarks can be made. A higher arousal level and the longer duration of this high arousal in novel situations might also be caused by a less efficiently functioning stimulus selection system. This may be so because, when animals have a less efficiently functioning filtration system, they will not be quick to distinguish the relevant and irrelevant aspects of the environment and, thus, will not be able to direct their behaviour as fast to the relevant stimuli. Konrad and Melzack (1975) suggest that a drastic change in environment confronts the organism with stimuli that are more or less meaningless. For the IC animals prior experience is comparatively useless in distinguishing whether social and physical stimuli are relevant or not. Under such circumstances the system fails through lack of experience that normally contributes to the selection and filtration processes in an early phase of the information processing, with the result that all stimulation reaches the brain and produces excessive arousal. In this framework the remarks of Melzack discussing his experimental results with respect to electrophysiological and behavioural effects of social isolation in dogs, are worth mentioning:

> "As a result of severe restriction of early sensory experience, most stimuli in a totally new environment have no meaning (phase sequences representing prior associations) to provide a basis for selective filtering of the sensory input. Consequently, all inputs, irrelevant as well as relevant, would reach the brain, where they could bombard the neural systems that produce

sensory and emotional arousal" (Melzack, 1969, page 727).

A second hypothesis proposes: rats that have been reared for some time in an impoverished environment, are less capable to inhibit responses (Ough et al., 1972; Morgan, 1973; Joseph and Gallagher, 1980). This hypothesis is based on the findings that IC rats perform less well in reversal learning tasks (Krech et al., 1962) and response transfer (Morgan, 1973), show slower extinction (Morgan, Einon and Morrison, 1977), over-respond on a two-lever DRL-schedule and thus get less rewards (Ough et al., 1972; Morgan, Einon and Nicholas, 1975), and learn a two-lever alternation more slowly (Morgan, Einon and Nicholas, 1975).
Situations in which response inhibition is studied, are often characterized in that next to response inhibition an efficiently functioning stimulus selection is involved also. The experiments of Lore (1969) and Melzack and Scott (1957) might serve as examples. Both studies reported that EC and IC animals did not differ with respect to pain-avoidance behaviour in the home cage, whereas in a novel situation the IC animals were less able to avoid pain stimuli adequately. Had the pain-avoidance behaviour been studied in a novel situation alone, the conclusion might have been that IC animals cannot suppress irrelevant responses very well. Since the pain-avoidance behaviour has been studied in both situations, it appears that the inadequate pain-avoidance behaviour in novel situations is caused rather by a less efficient stimulus selection, rendering the animal less capable of behaving adequately.

A third hypothesis assumes that animals that are reared in either enriched or impoverished environments differ in memory storage parameters (Greenough et al., 1972). Greenough et al. arrive at this conclusion on the basis of their data pointing out that SC mice perform as well as EC mice when spaced trials are given, but perform as badly as IC mice when massed trials are given (Greenough et al., 1972). Einon (1980) reported that animals reared in isolation learn a spatial memory task slower. However, she also observed that during the learning of this task the IC animals showed less systematic behaviour. Again, for the learning of a spatial memory task a well functioning stimulus selection mechanism is a necessary condition.

1.9. RESEARCH PROGRAMME

In the next chapters a number of experiments will be reported in which the behaviour of animals that have been reared in environments of differing stimuluscomplexities will be compared in a number of situations in which the efficiency of stimulus selection is an important aspect. In all the experiments described in this dissertation, up to the specific somatic or behaviour tests the same procedure has been followed as to group assignment and exposure to the various environments. This independent variable will be

described in detail in Chapter 2; a description of the environments used will be found there too.
Before starting with the experimental research which is described in the chapters 4, 5, 6 and 7, we decided to make sure whether exposing the animals to the environments we employed would produce effects on brain plasticity comparable to those frequently reported by the Berkeley group and others.
Thus, our first study focused on the problem whether the effect of prolonged exposure to environments of differing stimulus complexities on the weights of various parts of the brain, could be replicated (Chapter 3, experiment 1).
Subsequently, in chapter 4 a number of experiments are described that are concerned with habituation of locomotor activity in a novel environment, employing a forced-exploration situation as well as a free-exploration situation. A main feature of these situations is that the animals are confronted with an unfamiliar novel stimulus situation, which after a certain amount of time loses its novelty and relevance.
In chapter 5 a number of discrimination experiments are reported. A maze was used in which spatial as well as visual discriminative stimuli could be introduced. In the experiments described here, the amount of irrelevant stimulation was varied during the learning of the problem; the animals were confronted also with reversal problems. Main characteristic of a reversal problem is that stimuli that were relevant in first instance, are no longer so when the problem is reversed. The reversal problems employ intradimensional as well as extradimensional shifts.
In chapter 6, in a few experiments the question was investigated whether pre-exposure to the CS in the learning of a discrimination task affects the behaviour of EC and IC animals differently. Normally, pre-exposure to the CS used in a learning task, results in a decreased learning performance (Lubow and Moore, 1959; Lubow, 1973). This phenomenon is termed latent inhibition. One of the explanations proposed for this phenomenon (the non-associative interpretation) states that after pre-exposure the CS as a stimulus attracts less attention, and has less of a signal function (Mackintosh, 1973; 1975). In this way pre-exposure influences later stimulus selection. The CS is employed in a two-way active avoidance learning task in a shuttle box. The behaviour of animals with or without pre-exposure of the CS is assessed in the two-way active avoidance task.

Finally, this dissertation addresses itself to two different problems that play an important role in the research into the effects of differential experience on brain and behaviour.
The first problem is: which qualities of the differential experience are crucial for the development of the brain effects. More specifically, we investigated whether rearing in social isolation versus rearing in social groups would represent so much difference in stimulation as to produce brain effects comparable with those that result from rearing

in EC and IC environments. The Berkeley group maintain that social deprivation as opposed to social stimulation is not enough in itself to induce demonstrable brain changes. Stimulus enrichment by means of daily changes in the sensory environment via inanimate objects, in combination with an active tactile interaction with these objects, is a necessary condition to induce changes in brain functioning (Ferchmin and Bennett, 1975). However, research with e.g. monkeys demonstrates that social deprivation per se does produce neuroanatomical changes (for a review, see: Haracz, 1984). Stimulus enrichment might be realized by daily changing the social structure of the group of the socially reared animals. In the experiment reported here, it was investigated whether social isolation versus living in groups with or without a daily social enrichment would represent a large enough difference in experience to induce changes in brain variables (Chapter 3, experiment 2).
The second issue addressed is for how long after termination of exposure to the various environmental conditions behavioural effects can be demonstrated. This is a little researched topic, though studies have been done investigating how long after termination of the various environmental conditions and to what degree the differences in brain variables can still be demonstrated. It appears that after termination of the differences in environmental conditions, the differences in the brain variables disappear too in course of time (Bennett et al., 1974; Bennett, 1976). Apparently, the brain keeps adapting to changing circumstances. The quality of earlier environmental stimulation and the active interaction therewith may still have resulted in permanent changes in brain variables that cannot yet be measured, in which case these changes -long after the termination of a certain environmental condition- might still result in changed behaviour, for example in learning situations. In chapter 7 an experiment is described that aims to throw some light on the effect of pre-exposure of the CS in EC and IC animals, one year after termination of their living in different environments (Chapter 7, experiment 1).

CHAPTER 2

GENERAL PROCEDURE EMPLOYED IN ASSIGNING THE SUBJECTS TO THE VARIOUS CONDITIONS, AND DURING REARING

2.1. INTRODUCTION

In each experiment described in this dissertation, until the measuring of the effects of differential experience on brain and/or behaviour, the same methods are used with respect to group assignment as well as housing the animals in the respective environments. In order to achieve results that are comparable as much as possible with those of the Berkeley group, the enriched, standard and impoverished environments used here are almost identical with those employed by the Berkeley group (Rosenzweig and Bennett, 1969). In one of the experiments to be reported here (see chapter 3, experiment 2) the environments have been modified in order to investigate the underlying causes of the influences of enriched and impoverished environments on the brain of the rat.
To enhance the comparability of our experiments with those of the Berkeley group, the same strain of rats was used. In each experiment a new group of subjects was used.

2.2. SUBJECTS

In each experiment male rats were used of the Tryon Maze Bright strain (TMB, also called S1). This strain was bred around 1935 by Tryon (Tryon, 1940). Tryon started his selective breeding with an aselect group of 142 rats, males and females. Subsequently he selected them on the basis of their learning performance in a multiple-T maze. In the course of time, he thus obtained two strains: the Tryon Maze Bright (TMB, also called S1) and the Tryon Maze Dull (TMD, also called S3).
The animals used here have been bred at the animal laboratory of the Department of Comparative and Physiological Psychology at the University of Nijmegen.

2.3. ENVIRONMENTS

In the experiments described here a total of five different environments have been used.
- an impoverished condition (IC). The animals in this condition were housed individually in Macrolon cages of 38x27x15 cms. The IC cages were kept in a separate, quiet room. This environment is almost identical with the IC environment used by the Berkeley group.
- a standard laboratory condition (SC). In this condition three rats were housed simultaneously in Macrolon cages of 57x35x20 cms. The SC cages were placed in the same room as the EC cages. This environment is identical with the SC condition of the Berkeley group.

- an enriched condition (EC). In this condition a group of 10 to 12 rats were housed in a cage of 75x75x80 cms. The cage had metal sidewalls and backwall, a hinged perspex frontwall and a wired mesh roof. At the inside against one of the sidewalls there was a metal platform of 75x11 cms, 30 cm above the floor. This platform could be reached from the floor via a ladder. Two foodbowls and two waterbottles were placed against one of the sidewalls. Further, the cage contained six stimulus objects that were exchanged daily and chosen from a set of 30 objects (for example a green plastic tube, a wooden board, a yellow plastic runningwheel, a square metal box etcetera). This environment is almost identical with the one employed by the Berkeley group.
- a fixed group condition (FGC). This condition consisted of an EC cage without the stimulus objects. Each cage held 10-12 animals.
- a socially enriched condition (SEC). This condition employed four EC cages without stimulus objects. In each cage 12 rats were kept. Each day the group composition of the animals in the four cages was changed, resulting in a daily change of the social structure in each cage.

The floors of all cages were covered with sterilized saw dust. Ambient temperature in the rooms in which the cages were placed was kept at a stable level of 20° C. Food and water were available ad libitum.

2.4. PROCEDURE

From the time of weaning onwards to the end of the experiments, all rats were kept on a reversed day/night schedule, with the light on from 21.30 to 9.30 hour.
At an age of 28 days approximately, the rats were weaned, sexed and marked with an earmark; their weights were taken and they were assigned to the various environmental conditions. If, for example, an experiment used only two conditions, two males from each litter were semi-randomly assigned one to each condition. When an experiment employed three environments (IC, SC and EC; or IC, FGC and SEC) three male littermates were taken each time and divided semi-randomly over the three conditions. In every group assignment procedure the body weights of the animals were taken into account, so that the groups formed hardly differed as to mean and standard deviation of the body weights.

The animals stayed in their respective environments for at least 30 days, 24 hours a day. The weights of all animals were taken weekly. After termination of the periods in the various environments all animals were housed individually in Macrolon cages of 38x27x15 cms. Three days later they became available for somatic or behavioural tests.
During this somatic and behavioural research the animals had code numbers not related to the specific experimental

conditions they had stayed in. Thus, the experimenter did not know from which condition each individual came.

CHAPTER 3

EFFECTS OF DIFFERENTIAL EXPERIENCE (DUE TO REARING IN ENVIRONMENTS OF VARYING STIMULUS COMPLEXITIES) ON BODY WEIGHT AND REGIONAL BRAIN WEIGHTS

3.1. INTRODUCTION

Before starting our main research into the effects of differential experience on behaviour we wanted to know whether the environments we were planning to use would result in somatic effects similar to those described by the Berkeley group. In other words: does housing in our environments function in the same way as housing in the environments used by the Berkeley group, at least with respect to somatic variables that can be measured.
If housing in the environments we will use has the same influence upon the somatic substratum as does housing in the environments used by the Berkeley group, we will be able to compare the behavioural aspects we will study with the somatic effects that are obtained and will be obtained yet in Berkeley and elsewhere.
In this chapter data are represented on the effects of differential experience, through housing in the environments we use, on body weight (3.2) and on the weights of various parts of the brain (3.3. experiment 1 and 3.4. experiment 2).

3.2. EFFECTS ON BODY WEIGHT

3.2.1. INTRODUCTION

A large number of experiments have demonstrated that housing in environments of different stimulus complexities affects the body weight: animals housed in an impoverished environment develop higher body weights than those housed in an enriched environment (e.g. Zolman and Morimoto, 1965; Rosenzweig et al., 1971; Greenough et al., 1973; Morgan, 1973; Bennett et al., 1974; Fiala et al., 1977). This effect was found in several strains of rats, such as the TMB, TMD, Fisher, Spraque-Dawley, Long-Evans and Wistars (Bennett et al., 1964).
The effect reaches significance already after a few days stay (four days) in the environments concerned (Rosenzweig and Bennett, 1978); the difference is still present after a period of 160 days (Rosenzweig and Bennett, 1978) or even a year (Doty, 1972) in these environments. The effect has been found in young as well as older rats. Even rats that at an adult age had been placed in environments with differing stimulus complexities and had remained there for one year, differed from each other in body weight: again, the IC

animals had a higher body weight (+8%) than the EC rats (Doty, 1972).
A possible cause of the development and maintenance of this difference might be found in a difference in food consumption. If food consumption was inspected more closely, indeed, a difference was found: IC animals ate more than did the EC animals and this difference in feeding remained at a stable level during the entire period in the various environmental conditions (Baenninger, 1967; Sturgeon and Reid, 1971; Tagney, 1973; Fiala et al., 1977).
Our first somatically directed investigations were concerned with the development of the body weights of our subjects during housing in the various environmental conditions used (see chapter 2.3); the animals were kept in these environments for 30 days approximately. Following this study, we investigated whether after a more prolonged exposure, 90 days, to the environments used, the body weight differences between EC and IC animals still were present. At the same time food consumption was measured. Finally, it was investigated whether a shift of environmental condition after 90 days would also result in a change in food consumption and body weight.

3.2.2. METHODS

For all animals being reared in the various environmental conditions each week the body weights were measured. Subsequently, the group data were compared, taking into account that a split-litter design was followed by assigning the animals to their respective conditions (see chapter 2.4).
Three EC-IC groups, composed of 3x11 diplets were housed for 90 instead of 30 days from weaning onwards in the various environments. The weights of these animals were taken weekly also. Food consumption was measured per week. Food consumption of the EC animals was determined by averaging the food consumption of the entire group of animals in each EC cage.
After termination of the 90 days period of differential experience, the 11 animals of one EC condition were rehoused in an IC condition, whereas their IC littermates remained in the IC condition. After 19 days the weights of these subjects were taken and food consumption was measured again.

3.2.3. RESULTS

The results of the weight determinations of the animals housed for 30 days in the different environments, are shown in the tables 3.1, 3.2 and 3.3.
Table 3.1 has been derived from 540 subjects from 270 diplets. Of each diplet one rat was assigned to the EC condition, the other to the IC condition. At the moment the housing in the various environments started, both groups did not differ with respect to mean and standard deviation of body weight.

Table 3.1
Effects of differential experience in EC and IC environments, during 28 days from weaning onwards, on body weight

	days			
	7	14	21	28
EC vs IC	-8.9	-12.0	-12.2	-12.3

Percentage difference : $\frac{EC - IC}{IC} \times 100$

Table 3.2
Effects of differential experience in EC, SC and IC environments, during 28 days from weaning onwards, on body weight

	days			
	7	14	21	28
EC vs IC	-11.9	-14.5	-12.4	-13.1
SC vs IC	- 4.6	- 6.4	- 4.0	- 6.1
EC vs SC	- 7.7	- 8.7	- 8.7	- 7.5

Percentage difference : $\frac{EC - IC}{IC} \times 100$, $\frac{SC - IC}{IC} \times 100$, $\frac{EC - SC}{SC} \times 100$

Table 3.3
Effects of differential experience in SEC, FGC and IC environments, during 28 days from weaning onwards, on body weight

	days			
	7	14	21	28
SEC vs IC	- 8.1	-10.6	-10.4	- 9.7
FGC vs IC	- 8.5	- 8.6	- 8.8	- 9.0
SEC vs FGC	1.1	- 2.2	- 1.7	- 0.8

Percentage difference: $\frac{SEC - IC}{IC} \times 100$, $\frac{FGC - IC}{IC} \times 100$, $\frac{SEC - FGC}{FGC} \times 100$

Table 3.2. has been computed from 162 subjects from 54 triplets. One animal from each triplet was assigned to the EC group, another to the SC group and the third to the IC group.
Table 3.3 shows the results of 96 subjects from 32 triplets. The three animals of each triplet were assigned to SEC, FGC and IC conditions respectively.

From Table 3.1 it appears that IC animals develop higher body weights than their EC littermates do. Already after seven days each IC rat weighed more than his EC littermate, and this difference stayed at a stable level during the remaining period of 21 days. In tables 3.5 and 3.6 it is shown that after 35 days of differential experience IC rats have significant higher body weights compared with their EC and SC littermates; the latter, in turn weigh more than their EC littermates. Table 3.8 demonstrates that SEC animals and FGC animals do not differ in body weight after 30 days of differential experience. Both groups, however, do differ from their IC littermates, the latter being heavier. After being housed for 90 days in EC and IC environments respectively, the body weight differences between groups are still to be found: IC animals remain at a higher body weight level than their EC littermates (fig. 3.1).
Further, it appears that IC animals consume more food than their EC littermates do: the size of this difference remains almost the same throughout the entire period of 90 days (fig. 3.2). When after 90 days housing in an enriched condition the animals are rehoused in an IC environment, 19 days later their body weights do not differ any more from those of their IC litermates; their food consumption now is identical with that of their IC littermates also (see Table 3.4).

Table 3.4
Body weights (gs) and food consumption a day (gs) for EC and IC rats, 0 and 19 days after the end of their different environmental exposure from 25-115 days of age

	Body weight		
	0	19	Food consumption
EC	370	400	22.3
IC	395	399	22.3

3.2.4. DISCUSSION

Our data with respect to the effect of rearing in environments of varying stimulus complexities on body weight correspond with those frequently reported in the literature (Rosenzweig and Bennett, 1978). Animals housed in an impoverished environment develop a higher body weight in comparison with animals living in an enriched environment.

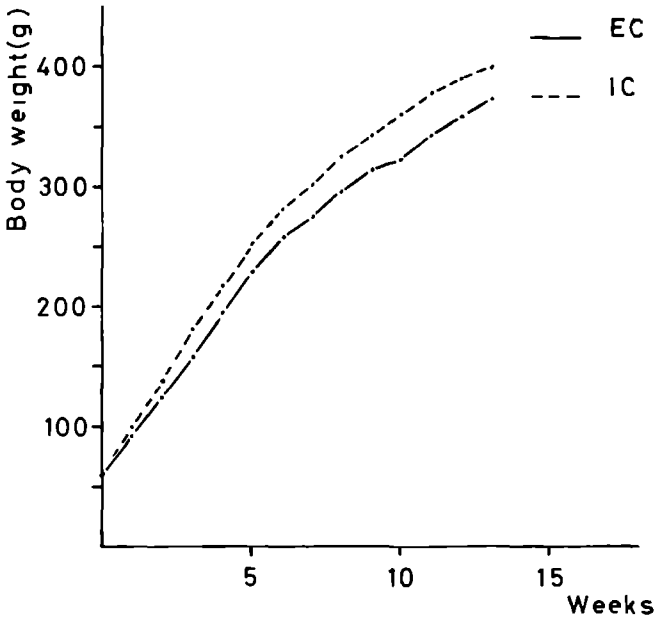

Figure 3.1. Mean body weight per week for EC and IC rats during a differential rearing period of 90 days, from weaning onward.

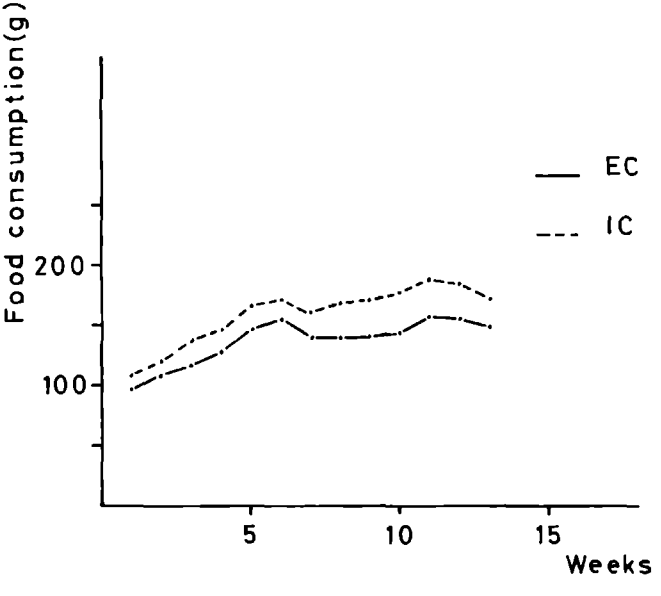

Figure 3.2. Mean food comsumption per week for EC and IC rats during a differential rearing period of 90 days, from weaning onward.

The findings that IC animals consume more food could be replicated also. We demonstrated that this difference remained during longer exposure to the various environments, measured here up to 90 days. The difference disappears when EC animals are transferred to an impoverished environment: food consumption and body weight are environment dependent. The amount of food regularly consumed by an animal (eating much versus eating little) is known to be a factor that may influence the brain. It has been reported that severe food restriction of animals in itself can reduce the degeneration of dopamine receptors in the striatum (Levin et al., 1981) The low food consumption in EC animals, then, might contribute to the development of the EC/IC effects on brain variables. Why animals in an IC environment eat more, is not clear. Fiala et al. (1977) suggest that perhaps boredom might play a part. Fiala also points out that EC rats have more opportunity for gnawing, namely at the objects. Indeed, in our EC environments the wooden objects have been gnawed away quite a bit after a while. However, a difference in body weight develops between FGC and IC animals also (both conditions consist of bare cages without stimulus objects), which indicates that a differing opportunity for gnawing does not have to be a causal factor.
In some of our experiments the behaviour of EC and IC rats in their respective environments has been observed during one hour per day, from 30 minutes before to 30 minutes after the start of the dark period. EC rats respond upon the change from light to dark with a sharp increase in locomotor activity: they start walking and running through the cage. IC rats show hardly any reaction at all: their locomotor activity remains low. Observations at other times during the dark period suggest that the locomotor activity of the EC animals in general is much higher than that of the IC animals. This might be one reason why EC rats have lower body weights in comparison with their IC littermates. IC rats, on the other hand, sometimes show a kind of emotional eruption: during a few minutes very fast movements may been seen, within those minutes a few times interrupted by freezing behaviour.
In general, it may be concluded that IC rats become heavier than EC rats. IC rats eat more in their impoverished environment than EC animals do in their enriched environment. This difference in feeding behaviour appears to be environment dependent.

3.3. EXPERIMENT 1*. EFFECTS OF DIFFERENTIAL EXPERIENCE IN ENRICHED (EC), STANDARD (SC) AND IMPOVERISHED (IC) CONDITIONS ON THE WEIGHT OF VARIOUS PARTS OF THE BRAIN

3.3.1. INTRODUCTION

As reported already in chapter 1 housing in environments of varying stimulus complexities has effects on a variety of neuroanatomical and neurochemical variables (see chapter 1).

Animals that have been housed for a long time in an enriched environment (EC), develop among other things heavier cortex parts, particularly the occipital cortex, compared with animals that have been kept during the same time in impoverished conditions (IC).
The aim of this first experiment was to investigate whether the environmental conditions we used might reproduce any of the above-mentioned effects of housing in the EC, SC and IC environments of the Berkeley group. Thus, in this experiment the influences of these three types of environments upon the weights of various parts of the cortex as well as upon the weight of the entire cortex, the cerebellum, hippocampus, striatum, the pontic-medullar area, the entire subcortex, the entire brain and the cortex/subcortex weight ratio were determined. The latter variable, the cortex/subcortex ratio, has been used frequently by the Berkeley group. This variable reveals one of the most consistent differential experience effects: it appears that the cortex weight increases as a result of housing in an enriched environment, whereas the weight of the rest of the brain hardly changes (Rosenzweig et al., 1972b).

3.3.2. METHODS

Subjects

The subjects were 36 male TMB rats in 12 sets of three littermates each. The rats were weaned at an age of approximately 30 days and subsequently housed in either an EC, SC or IC environment during 35 days. Each condition contained 12 rats. A description of the environments and the general procedure per condition is given in chapter 2. After a period of 35 days in the various environments all animals were rehoused and placed individually in IC cages. Within three days the animals were sacrificed.

Procedure

All dissections were performed by an experimenter who didn't know the condition each individual came from.
The rats were weighed immediately before being decapitated. After decapitation the head was kept about 5 sec. in liquid nitrogen to cool the brain. Further preparation was done in the cold (ca 6° C). The skin and dorsal skull were removed and guided by a plastic T-square identical to that used by the Berkeley group transverse as well as lateral incisions were made as indicated in Bennett et al. (1964) and Raaijmakers (1978), and the occipital, somesthetic and remaining dorsal cortex were dissected. The remaining dorsal cortex is laterally bordered at the rhinal fissure, since

* The experiments 1 and 2 have been executed in close cooperation with dr. W.G.M. Raaijmakers, who determined i.a. effects on AChE-activity in various parts of the brain (Raaijmakers, 1978).

this fissure separates neocortex from paleocortex (cortex samples can be cleanly pealed from the underlying white matter, since in the brain there is a clear mechanical gradient between these two kinds of tissues). After removing the cerebellum, the ventral cortex (comprising i.a. pyriform cortex, amygdala and enthorinal cortex) and the hippocampus were dissected free. The striatum was dissected free from capsula interna and the septal area. The remaining tissue was divided into two parts by a transverse cut just rostral to the pons. The caudal part consisted of pons and medulla, the frontal part consisted of i.a. the thalamus and the rest of the brain.
The brain regions were immediately wrapped in pre-weighed pieces of aluminium foil, weighed and frozen in liquid nitrogen. They were stored in closed vials at -74° C until analyses were made.

3.3.3. RESULTS

One rat had to be discarded because of a decapitation fault that damaged the cerebellum and medulla oblongata.
Thus, all results have been based upon 11 sets of three littermates each (11 triplets). Group means of all weight variables are presented in Table 3.5. This table also gives F-ratios from the analyses of variance. These analyses of variance reveal that the various environments caused significant group differences with respect to weight of occipital cortex, total neocortex weight, neocortex/rest of brain weight ratio, and total brain weight.
Post-hoc analyses were performed in order to determine which groups differed significantly from each other. These post-hoc analyses were done by using the Scheffe contrast method on the means. Table 3.6 depicts the results. As for the weight of the occipital cortex, group EC differs from group IC (EC>IC, 12.6%) and group EC almost differs from group SC (EC>SC, 9.8%, $p<.07$). As for the dorsal neocortex, group SC differs from group IC (SC>IC, 4.5%).
Further, it appears that the difference in total neocortex weight between the EC and IC groups reaches significance (EC>IC, 4.3%) and between the SC and IC groups as well (SC>IC, 3.1%). In total brain weight group SC and group IC differ also (SC>IC, 2.4%). The neocortex/rest of brain weight ratio of group EC is larger than that of group IC (3.8%).

3.3.4. DISCUSSION

Housing TMB rats during 35 days in the environmental conditions used here, besides having an effect upon body weight also affects the weights of various parts of the brain. The results of experiment 1 quite nicely fit the pattern produced by the Berkeley group (Zolman and Morimoto, 1965; La Torre, 1968; Huntley and Newton, 1972; Globus et al, 1973; Bennett, 1976; Diamond, 1976; Rosenzweig and Bennett, 1978). Just like this group of scientists we found

Table 3.5
Mean brain weights (mgs) and body weights (gs) for 11 littermate triplets of male TMB rats, after 35 days of differential experience in EC, SC, and IC environments from weaning onwards

	EC	SC	IC	F-ratio
	$\bar{X}$ ± SEM	$\bar{X}$ ± SEM	$\bar{X}$ ± SEM	(df 2,20)
Occ. cortex	87.4 ± 3.1	79.6 ± 2.3	77.6 ± 3.0	5.944 **
Som. cortex	61.2 ± 2.0	57.3 ± 1.6	58.9 ± 1.9	1.698
Dors-rest cortex	302.0 ± 5.1	308.6 ± 5.1	295.4 ± 5.8	4.740 *
Total (X)	450.6 ± 7.0	445.5 ± 6.7	431.9 ± 7.2	9.511 **
Ventral cortex	233.1 ± 3.5	240.5 ± 5.3	234.9 ± 4.8	0.926
Cerebellum	248.8 ± 1.9	250.1 ± 2.1	248.2 ± 3.0	0.310
Hippocampus	93.5 ± 1.7	95.4 ± 2.1	95.1 ± 1.9	0.239
Striatum	177.4 ± 3.0	180.8 ± 3.8	172.6 ± 4.8	1.379
Pons-medulla	137.8 ± 2.4	143.2 ± 3.3	142.4 ± 5.3	1.045
Rest subcortex	281.9 ± 2.9	281.4 ± 3.0	274.1 ± 3.2	2.218
Total (Y)	1172.5 ± 11.8	1191.4 ± 9.5	1167.4 ± 10.3	2.098
Total brain (X+Y)	1623.1 ± 11.2	1636.9 ± 13.8	1599.3 ± 17.0	3.742 *
Ratio X/Y	.384 ± .006	.374 ± .005	.370 ± .006	4.826 *
Body weight	262 ± 4	291 ± 5	306 ± 5	44.831 ***

* $p < .05$ ** $p < .01$ *** $p < .001$

Table 3.7
Percentage differences in brain weight (mgs) and body weight (gs) among EC and IC rats, reared by the Berkeley group and by us (experiment 1); and among SEC and IC rats (experiment 2)

	Berkeley experiments n = 87	exp. 1 n = 11	exp. 2 n = 12
	EC vs IC	EC vs IC	EC vs IC
Occ. cortex	9.4	12.6	8.8
Som. cortex	3.6	3.9	10.9
Dorsal cortex	3.7	2.2	4.5
Total cortex (X)	4.2	4.3	6.5
Rest of brain (Y)	-0.9	0.4	0.2
Total brain	1.3	1.5	1.8
Ratio X/Y	5.1	3.8	6.2
Body weight	-11.0	-14.4	-8.6

$$\text{Percentage difference} : \frac{EC - IC}{IC} \times 100$$

Table 3.6
Post-hoc analyses of mean values (Scheffe contrasts)

	critical difference value	pair wise comparison		
		EC-IC	EC-SC	SC-IC
Occipital cortex	7.9	9.8	7.8	2.0
Dorsal cortex	11.3	6.6	4.6	13.2
Total neocortex	11.6	18.7	5.1	13.6
Total brain	36.6	23.8	13.8	33.6
Ratio X/Y	.012	.014	.010	.004
Body weight	12	44	29	15

Differences between two means exceeding the critical value indicate that the two means are significantly different ($p<.05$)

the largest percentual effects in the occipital cortex. Environmental enrichment enhances the weight of the occipital cortex as well as the weight of the remaining dorsal cortex. The latter effect, however, is percentually smaller than the effect upon the occipital cortex. The correspondence of our data with those of the Berkeley group is shown in table 3.7: this table compares the weight differences, expressed as percentages, for the various parts of the brain, as found by the Berkeley group and in the present experiment. The data of the Berkeley group are based on 87 littermate sets of male S1 rats that were housed in the various conditions from 25 to 55 days of age. In the data published by the Berkeley group and others as well, percentually small differences, e.g. in total brain weight, reach significance in some of their experiments. This appears to depend largely on the number of animals used per condition. However, these differences are nevertheless consistently found over a large number of experiments; presumably, in the separate experiments the small number of animals used prevents the relatively small differences to reach significance.
No effects were found on the weights of subcortical structures. This again replicates the Berkeley results. It appears that the increase in brain weight as seen in the EC group, compared with the IC group, is not the result of a gain in body weight. On the contrary: isolated animals developed a higher body weight on the one hand and a lower brain weight on the other, when compared with animals reared in an enriched environment.
Thus, it may be concluded that housing TMB rats in the environments used by us and those used by the Berkeley group influences brain structure in the same way.

3.4. EXPERIMENT 2. EFFECTS OF DIFFERENTIAL EXPERIENCE IN SOCIALLY ENRICHED (SEC), FIXED GROUP (FGC), AND IMPOVERISHED (IC) CCONDITIONS ON THE WEIGHT OF VARIOUS PARTS OF THE BRAIN

3.4.1. INTRODUCTION

In the research into the effects of housing in environments of varying stimulus complexities on brain and behaviour, a few studies aimed to discover which factors are responsible for the development of the effects (see chapter 1, 1.6). From these studies it may be concluded that the fundamental difference between the EC and IC conditions lies in the EC animals' opportunity for active interaction with daily changing objects. Thus rearing subjects in IC cages which were placed in EC cages did not affect the brain of those animals, in comparison with subjects of the normal IC condition, whose cages were stored in a separate quiet room (Ferchmin and Bennett, 1975).
Whether housing in social groups per se would suffice to induce significant quantitative effects, isn't clear. Initially, Rosenzweig and Bennett decided on the basis of

their results that social stimulation versus isolation was not sufficient to produce the usual EC/IC effects on brain values. Thus, in earlier publications they concluded that social stimulation in the EC condition played a role in the sense that it increased the amount of contact the animals had with the objects in the cage, and that only in that way it contributed to the development of EC/IC effects. Social stimulation alone as opposed to social isolation was not considered to have any effects on neuroanatomical and neurochemical variables (Rosenzweig and Bennett, 1972). However, in later publications of the Berkeley group it is remarked that "social stimulation does play an important role but does not produce the whole effect" (Bennett, 1976, pag. 284); from the experiments conducted it became clear that "housing animals in groups of 12 in a relatively large laboratory cage leads to cerebral changes in comparison with littermates housed individually in a small colony cage: significantly larger brain effects can be produced by presenting the 12 animals with a more complex environment" (Rosenzweig et al, 1978, pag. 573). Further, the Berkeley group concludes that the size of the brain effects varies in accordance with the complexity of the inanimate stimulus condition (Rosenzweig et al., 1978).
However, the Berkeley experiments do not necessarily give the impression that the EC/IC effects are caused predominantly by the presence of inanimate stimuli; they rather suggest that the amount and variety of the total stimulation, inanimate as well as animate, with which the animal can actively interact is the primary factor. This variation and amount of stimulation may be reached not solely through inanimate stimulation, but might be produced also by daily varying the social structure.
It appears that daily variation in the stimulation is an important factor in the development of the brain effects, whereas the literature stresses predominantly the variation in animate stimulation (Brown, 1971; Ferchmin and Bennett, 1975; Walsh and Cummings, 1975; Rosenzweig et al., 1978). In our opinion, a comparable daily variation in stimulation might also be produced by a daily variation of the social structure of the group.

In this experiment it was investigated whether social stimulation through rearing in a group of 12 animals versus social isolation would represent a large enough stimulation to produce brain effects similar to those found in experiment 1. Should this be the case, then this would enable us to implicate the results of investigations into the effects of social deprivation versus group housing upon behaviour in our research. A large amount of research into the effects of social deprivation versus social grouping upon later behaviour has been carried out especially by a group of scientists at the University of Cambridge (i.a. Einon, Iversen, Morgan and Sahakian).
Besides using a group with a fixed social structure we decided to introduce a group with enriched social stimulation through daily changing this social structure. Thus, we planned to investigate also whether a daily change

in social stimulation might play the same role as the daily changing of stimulus objects that in experiment 1 as well as in the expperiments of the Berkeley group apparently were so crucially important.

3.4.2. METHODS

Subjects
Thirteen sets of littermate triplets of male TMB rats were used. After weaning around the 25th day of age, the subjects were assigned to the three conditions SEC, FGC and IC. A description of the environments as well as the general procedure followed in group assignment and housing the animals in the various environments can be found in chapter 2. After 30 days of housing in their respective environments, all subjects were rehoused, by placing them individually in IC cages; within three days all animals were sacrificed.

Procedure
Weighing and storage of the samples was done as described before (3.3.2).
In this experiment, the subcortical part was devided in pons-medulla and rest of the subcortex (this part included ventral cortex, hippocampus, striatum and rest subcortex of experiment 1).

3.4.3. RESULTS

One rat had to be discarded because of hydrocephalus. All results are based upon 12 littermate triplets. The group means of all weight variables are presented in table 3.8.
The question whether social isolation versus rearing in social groups plays a role in the development of effects of differential experience on brain values, was investigated by comparing the IC group with both other groups combined (Comparison 1: IC versus (SEC+FGC)). The question whether a daily change in stimulation plays a role in the development of the brain effects, was investigated by comparing group SEC with group FGC (Comparison 2: SEC versus FGC).
The two comparisons were investigated with an analysis of variance. The results are presented in Table 3.8. Concerning the first comparison (IC versus (SEC+FGC)) significant effects of the condition on the weight of the occipital cortex, the somesthetic cortex, the whole neocortex, the whole brain and the neocortex/rest of brain weight ratio were revealed.
Animals reared in social groups apparently have a heavier occipital cortex, somesthetic cortex and total neocortex than have animals reared in isolation. Also the total brain weight of the subjects reared in groups is larger. The neocortex/rest of brain weight ratio of the IC animals is smaller.
The second comparison (SEC versus FGC) did not reveal any environmental effect. For a comparison of the percentage

Table 3.8
Mean brain weights (mgs) and body weights (gs) for 12 littermate triplets of male TMB rats, after 30 days of differential experience in SEC, FGC, and IC environments from weaning onwards

	SEC	FGC	IC	Analysis of variance I	Analysis of variance II
	$\bar{X}$ ± SEM	$\bar{X}$ ± SEM	$\bar{X}$ ± SEM	(df 1,23)	(df 1,23)
Occ. cortex	81.6 ± 2.4	79.3 ± 1.4	75.0 ± 2.4	4.87 *	0.57
Som. cortex	76.3 ± 2.5	74.0 ± 1.2	68.8 ± 2.3	5.54 *	0.56
Dorsal cortex	254.1 ± 8.5	249.6 ± 5.3	243.2 ± 5.1	3.77	0.71
Total (X)	412.0 ± 9.0	402.9 ± 5.3	387.0 ± 8.0	14.50 ***	2.17
Cerebellum	228.8 ± 4.1	232.2 ± 3.0	229.9 ± 3.0	0.04	0.96
Pons-medulla	154.2 ± 6.2	149.0 ± 4.6	155.4 ± 5.9	0.45	0.63
Rest of brain	767.4 ± 6.4	770.0 ± 6.2	76.32 ± 7.7	0.55	0.09
Total (Y)	1150.4 ± 9.9	1151.2 ± 10.6	1148.5 ± 10.1	0.06	0.01
Total brain	1562.4 ± 15.4	1554.1 ± 13.2	1535.5 ± 15.1	4.36 *	0.44
Ratio X/Y	.358 ± .007	.350 ± .005	.337 ± .006	9.57 **	1.57
Body weight	222 ± 7	225 ± 6	243 ± 6	13.44 **	0.23

* $p<.05$ ** $p<.01$ *** $p<.001$

differences between SEC and IC animals and the EC and IC animals of the first experiment and those of the Berkeley group, the reader is referred to table 3.7.*

3.4.4. DISCUSSION

Inspection of the results of this experiment reveals that animals reared for 30 days in a social group placed in bare EC cages as well as animals reared in EC cages containing a daily varying choice of objects, develop almost similar brain weight differences in comparison with isolated animals. It may be concluded then, that social stimulation in itself in contrast with social isolation produces so much difference in experience, that effects comparable with the EC/IC effects are the result. Enhancing social stimulation by daily changing the social structure of the group does not significantly affect the brain variables concerned (see footnote). A certain amount of stimulation (either via inanimate objects or living organisms) per day, together with the opportunity for active-tactile communication (called "experience") with those stimuli, apparently is a factor of crucial importance for the induction of brain effects compared upon the isolated group. Apparently, social stimulation is as effective as stimulation via inanimate objects. A larger social group offers more opportunity for varied stimulation with which the rat can interact in an active-tactile manner.
In the orignel EC condition as well as in the here introduced SEC and FGC conditions this opportunity is larger than in the SC condition. The factor "amount of active-tactile communication with stimuli", the term amount signifying variation, runs from low (IC) to high (SEC and EC). It appears that this factor plays a primary part in the development of effects on neuroanatomical and neurochemical and neurophysiological variables, induced by housing in environments of varying stimulus complexities.
On the same line are the results of Kuenzle and Knusel (1974) who designed a "super"-enriched environment that caused still larger differences from the IC group, compared with a "normal" EC condition. Some experiments of the Berkeley group also point in this direction: rats living in a semi-natural environment (SNE, offered even more variation in stimulation with opportunity for active interaction than the EC condition) developed a heavier occipital cortex

* One of the SEC animals had very low weight values for the occipital cortex and somesthetic cortex: 30% (and more than 5 s.d.) less than the mean of the rest of the group. If this rat, together with its FGC and IC littermates, is discarded from the results and if the analyses are based on 11 triplets, the SEC and FGC groups differ significantly from each other in weight of total neocortex ($F1,10 = 6.04$; $p < .05$).

etcetera in comparison with EC animals (Bennett, 1976; Rosenzweig and Bennett, 1978).
There appears to be, then, a sort of continuum, where the natural environment enables the development of a very high level of experience and the SNE, EC, SC and IC environments respectively represent environments of increasing impoverishment, that offer less and less opportunity for experience.
Initially, the Berkeley group did not find any effects on brain variables induced by social grouping in comparison with rearing in impoverished, socially deprived environments, though later on they did find such effects (smaller than ours).
A possible explanation for this (suggested by Raaijmakers, 1978) might be that in their earlier experiments they did not employ the split-litter design. Our experiments have shown that the between-litter variance can be so large as to completely mask potential differences induced by differential experience, because the error component of the variance is sharply enhanced (Van der Staay and Van Attekum-Hendriks, 1978).

CHAPTER 4

EFFECTS OF DIFFERENTIAL EXPERIENCE IN ENRICHED (EC) AND IMPOVERISHED (IC) ENVIRONMENTS ON HABITUATION

4.1. INTRODUCTION

In chapter 1 we formulated the assumption that EC animals and IC animals differ in the efficiency of the processes of stimulus selection and filtration of irrelevant stimuli. A possible approach to study this closer is to examine the habituation processes in EC as well as IC animals. Habituation may be defined as a decrement of an unconditioned response when the execution of this response obviously is not biologically relevant (Vossen, 1973). Habituation is investigated, among others, by measuring the response reduction in function of either continous or repeated exposure to an unchanging stimulus configuration. Through repeated or continous presentation, the stimulus configuration gradually loses its relevance features: a transition from relevance to irrelevance occurs, which induces a decrease in responding. This decrease might be measured within-session (short-term habituation) as well as over a number of sessions that are separated by different stimulus-situations (between-session: long-term habituation). There are good reasons for the assumption that short-term habituation and long-term habituation do not represent the same process. Studies employing drugs, neural lesions and behavioural manipulations suggest that short-term habituation and long-term habituation are differently affected by these interventions and may be independent processes that probably reflect the activity of different neural systems (Rinaldi and Thompson, 1985).
Two types of behaviours often used in habituation experiments are activity in the open field and the startle response. Activity in the open field is studied by giving the animals a number of opportunities to remain in the open field for a certain amount of time (for example 25 min.). The decrease of locomotor activity in this open field is then considered a measure for the rate of habituation. The decrease of locomotion may be measured during a forced stay in the open field or during a period in which the subject has free access to the open field. Whereas in a forced exposure the animals initially show a high level of locomotor activity that gradually decreases, in a free access situation this decrease occurs only after a gradual increase in locomotor activity (Welker, 1957; Aulich, 1976). A second procedure to study habituation processes is to measure the amplitude of startle responses to aversive acoustic stimuli. Attenuation of the startle response is taken as a measure of the rate of habituation.
Are both types of habituation different? Several investigations suggest that this is the case. Differences between habituation to novel environments and habituation to intense acoustic stimulation have been found, and it has been suggested that the habituation of these two types of

responses are mediated by different processes (Williams et al., 1974). Thus, it was found that an inhibition of the activity of the cholinergic system abolishes the decrease in locomotor activity in the open field over a period of 30 minutes (short-term habituation), whereas animals that had been administered saline or methscopolamine still did show a significant decrease (Grant, 1974). Williams et al. (1974) also reported that scopolamine retarded the decrease in responding in exploratory situations, though they did not find an effect of scopolamine upon the attenuation of the startle response. The latter finding was also reported by Warburton and Groves (1969). These differences in results support the hypothesis that habituation to these different stimulus situations is mediated by different processes (Williams et al., 1974). It has been suggested that this discrepancy results from differences in the experimental procedures employed. In the startle response habituation experiments discrete startle reactions to discrete stimuli are measured, whereas in open-field habituation experiments a reduction of activity is measured in function of a continuous exposure to the novel stimulus situation (Van der Staak, 1976). The sensitivity of open-field habituation to interventions in the cholinerg system has not been demonstrated by the studies of Grant and Williams et al. only, but has been hinted at by other data also: habituation (measured as a decrease in locomotor activity in the open field) appears around the third or fourth week in the rat's ontogeny and, thus, runs parallel with the development of the cholinergic system (Campbell et al., 1969; Feigly et al., 1972; Bronstein et al., 1974).
The object of the experiments reported here is to investigate the development of habituation in EC as well as IC animals by studying both the decrease of locomotor activity in the open field (experiments 1, 2 and 3) and the reduction of startle responses (experiment 4).

Departing from the hypothesis that in EC and IC animals the cholinergic system functions differently, and, hence, there is a difference in the efficiency of stimulus selection (chapter 1, 1.8); and considering also the above-mentioned data concerning cholinergic influences upon the habituation process concerned here, we might expect

a) that EC and IC animals do differ in rate of habituation in the open field, as revealed by a decrease in locomotor activity; IC rats will habituate slower to the open field than EC rats,
b) that no differences between IC and EC animals will be found in the rate of habituation to an intense aversive acoustic stimulus, as revealed by attenuation of the startle response.

4.2. EXPERIMENT 1. EFFECTS OF DIFFERENTIAL EXPERIENCE IN ENRICHED (EC) AND IMPOVERISHED (IC) ENVIRONMENTS ON THE HABITUATION OF ACTIVITY IN THE OPEN FIELD

4.2.1. INTRODUCTION

Rearing in an enriched (EC), impoverished (IC) or standard laboratory environment (SC) appears to influence locomotor activity in a novel environment, as, for example, the open field. A large number of researchers have reported that animals reared in either enriched or standard laboratory environments showed more activity in the open field than animals from impoverished conditions (Lore and Levowitz, 1966; Levitsky and Barnes, 1972; Smith, 1972; Syme, 1973). Other researchers, however, found no differences (Denenberg and Morton, 1962; Joseph and Callagher, 1980) or even obtained an opposite difference (Zimbardo and Montgomery, 1957; Woods et al., 1960; Morgan, 1973; Einon et al., 1975; Einon and Morgan, 1978b). It might, however, be questioned in how far the many studies of this topic can be considered comparable. It appears, that large differences exist with respect to the types of rearing conditions used, as well as the test situation, duration of exposure to the test situation, etcetera, which renders the results rather difficult to interpret and to compare. For example, differences in results might arise when EC, SC and IC animals differ as to the rate at which the locomotor activity in the open field decreases. A short or long period in the open field will then result in differences between the EC, SC and IC animals with respect to the total amount of activity that can be measured.
The rate of decrease of the locomotor activity in the open field has been studied several times. Such research is of importance in relation with the hypothesis formulated in chapter 1, that EC and IC animals differ as to the efficiency of their stimulus selection processes. On the one hand, a less efficient stimulus selection might mean that in a novel situation the animal cannot distinguish relevant and irrelevant aspects as fast (that is, the inhibition related to irrelevant stimuli does not function as well). On the other hand, an inhibitory system that does not work optimally with respect to irrelevant stimuli might also have the effect that once relevant stimuli keep their novelty and relevance features for a longer time, that is, do not become irrelevant as fast, so that the subjects go on responding to those stimuli for a longer period of time. Research into rate differences in the decrease of locomotor activity in the open field suggest that IC and SC animals do not differ in this respect, as measured by exposure to the open field during three minutes per day over four days (long-term habituation; Studelska and Kimble, 1979), and as measured by a period of one hour in the open field (short-term habituation) as well (Einon and Morgan, 1978b). However, Sahakian et al. (1975) reported that IC animals did show a faster decrease in locomotor activity as compared with SC, when measured during a two-hour period in photo-cell cages.

On the other hand, it was found that EC animals, compared with IC animals, showed a faster reduction of locomotor activity in the open field when measured during three minutes per day, over four days (Studelska and Kimble, 1979), as well as when measured during a period of 20 minutes in the open field (Domjan et al., 1977). Thus, it seems that EC animals indeed show a faster decrease of locomotor activity in the open field.
As to the meaning of this locomotor acitivity in the open field two opinions prevail. On the one hand, it is considered a representation of exploratory behaviour (Vossen, 1966; Russell and Williams, 1973), and on the other hand it is thought to represent emotionality and escape behaviour (Blanchard et al., 1974), particularly so during the first trial (Whimbey and Denenberg, 1967; Denenberg, 1969). The effects of differential experience on exploratory behaviour have been studied not only through open-field activity, but also in other ways, for example, through measuring the duration of manipulation of novel objects, or, the amount of time spent in environments containing novel objects, as compared with the amount of time spent in empty bare environments, etcetera.
Initially, it was reported mainly that IC animals had a higher exploratory drive than animals reared in more enriched environments (Zimbardo and Montgomery, 1957; Woods et al., 1960; Denenberg and Grota, 1964; Lore and Levowitz, 1966; Sahakian et al., 1977). Studies of the rates of decrease of exploratory behaviour towards novel stimulus objects almost invariably demonstrated a slower decrease in IC animals than in animals reared in more enriched environments, in either SC or EC (Konrad and Bagshaw, 1970; Manosevitz and Joel, 1973; Einon and Morgan, 1976, 1977; Sahakian et al., 1977; Joseph and Gallagher, 1980). Significantly, a few researchers remarked that though IC animals maintained a high level of exploratory activity in the presence of novel stimuli, this exploratory behaviour was much less systematic, functional and adequate than the exploratory behaviour by animals from more enriched environments (Konrad and Bagshaw, 1970; Einon and Morgan, 1976; Joseph and Gallagher, 1980). Thus, it has been observed, that IC animals do not show very well adapted behaviour towards novel stimuli: they "overreact" to the new stimuli and lapse into persevering repetitive responses, wich indicates a deficit in the capacity to selectively pay attention to novel stimuli for a long enough period of time (Joseph and Gallagher, 1980, page 535). Melzack (1969) noted that IC dogs did not explore new objects selectively, but performed exploratory movements without intention. Upon repeated confrontations with the same stimuli the IC dogs responded as if the stimuli were entirely novel to them. In other words, these data suggest that IC animals explore longer not so much because of a higher exploratory drive, but because they are less capable to employ an effective stimulus selection. Repeated or continuous exposure to novel stimulation results in a slower habituation to and a slower integration of this stimulation in these animals.

Returning to the locomotor activity in the open field, the above-mentioned effects warrant the assumption that EC and IC animals differ in rate of decrease of locomotor activity, within as well as between sessions. The experiment described here aims to examine this. To this end a sufficient duration of observation of the locomotor behaviour per session will be employed. In connection with remarks made by several researchers (Melzack, 1969; Einon, 1980; Joseph and Callagher, 1980) with respect to the less systematic behaviour of IC animals, not only locomotor activity will be recorded, but other behavioural variables, such as sniffing, rearing, grooming etcetera will be considered also.

4.2.2. METHODS

Subjects

In this experiment 20 male TMB rats were used. At the time of testing the animals were ± 65 days of age. 10 Subjects had been reared in an EC environment, their 10 littermates had been reared in an IC environment. Subjects had been weaned at an age of 25 days. Immediately after weaning, they had been placed in the various environments, in which they remained for 42 days continuously. Subsequently, they had been housed individually and three days later the testing procedure started (For a more extensive survey of the pre-experimental procedure, see chapter 2).

Apparatus

The open field consisted of a wooden cage of 100x100x34 cms, painted light grey. One of the sidewalls as well as the cover (which contained air holes) was made of plexiglass. The floor was divided in 36 squares of 16.7x16.7 cms each by black lines. The open field was situated in an empty experimental room which was illuminated by a red bulb of 40 W, hanging approximately 100 cms above the open field. The behaviour of the animals in the open field was observed from an adjacent room through a one-way screen.

Procedure

All subjects were tested individually, during 25 minutes per day (one session) on four consecutive days. All testing took place in the dark period of the 24 hours light/dark cycle. Littermates were tested one immediately after the other. The observer was not aware of which animals belonged to the EC condition and which to the IC condition. A session proceeded as follows. At the start of each session the rat was placed in the center of the open field. One minute later behaviour observations began. A time sampling method was employed. A complete description of this method may be found in Vossen (1966). In short, this observation procedure was as follows: during the observation period of 25 minutes, each tenth second an observation was made. The following aspects were recorded:

- the square the rat was in;
- the behaviour the animal was involved in.

As to the determination of the exact location the animal was in, the square in which it had most of its legs was taken. In case the animal was in two squares, each square containing two of its legs, or in case the four legs were placed in four different squares, the square containing its left hind leg was chosen as the animal's location.
In recording the animal's behaviour a choice was made out of a total of nine behaviour categories:
W: Walking; the rat walks or changes position by moving at least three of its legs;
S: Sniffing; the rat sniffs, licks or bites a part of the open field;
T: Sniffing; the rat sniffs the air;
R: Rearing; the animal rears on its hindlegs, its frontlegs placed against the sidewall.
O: Rearing; the animal rears on its hindlegs, without support for its frontlegs.
G: Grooming; grooming the head: scratching or cleaning the head, usually with the frontpaws.
P: Grooming; grooming the rest of the body: scratching, licking and biting the body.
Z: Sitting/lying; the animal sits motionless on the floor or lies in an asymmetrical posture with its belly on the floor, head down.
If at a given moment W as well as S or T were performed, or R as well as S or T, or O as well as S or T, only W, R and O respectively were recorded. If R occurred together with G or P, or O together with G or P, only G or P were recorded. A session's duration was 25 minutes; thus 150 observations were obtained per session. After each session the animal was removed from the open field and returned to its home cage.

4.2.3. RESULTS

The amount of locomotor activity in the open field of a given rat was computed in three ways:
1. by calculating the number of shifts of position;
2. by calculating the distance travelled;
3. by calculating the frequency of occurrence of behavioural category W.

The number of shifts of position was calculated as follows: for each two consecutive observations it was determined whether or not in the intervening 10-seconds period the rat had moved to another square of the open field. In each session a maximum of 149 shifts of position could occur.
The distance travelled was calculated by means of the city-block method (Vossen, 1966). At each moment of observation the minimum number of squares was determined which the animal had to traverse in order to get from the square where it was in at observation moment x to the square it was in at the observation moment x + 10 seconds. To this end it was determined how many squares had to be crossed over the lenght and width of the box in order to get from one place in the open field to the other (Vossen, 1966). The distance travelled between two observations is defined as the theoretically minimal number of squares crossed.

To examine short-term habituation each session was divided in three periods of 50 observations, lasting 8 minutes and 20 seconds each.
Table 4.1 contains the mean distance travelled (A), mean number of shifts of position (D) and frequency of the behavioural categories W, R, O, S, T, G, P and Z per period per session. Totals per session and totals over sessions are given also. Results from the analyses of variance performed on these data, are represented in Table 4.2.
First, the main effects will be dealt with. A differential experience main effect was found only in the category Walking: IC rats ambulate more than EC rats do during the total of 100 minutes of observation in the open field. The main effect of differential experience almost reaches significance (IC>EC, $p<.07$) in the number of shifts of position (D). Examing the session main-effect, the number of shifts of position (D) decreases significantly over the sessions; the frequencies of S (sniffing) and P (grooming body) decrease also, whereas Z (sitting/lying) increases in frequency. The behaviours W (walking) and G (grooming head) increase slightly too, but these increases do not reach significance ($p<.07$).
A significant main effect of period of session was found for all variables. Within-session, distance travelled (A) and number of shifts (D) decrease, as do the frequencies of behavioural categories W, R, O, S, T and G. Only categories P and Z show increases within a single session of observations.
More important for our research, however, are the interactions between the factors period and environment (within-session or short-term habituation), as well as the interactions between the factors session and environment (between-session or long-term habituation). The interaction between the factors environment and period indicates whether EC and IC animals differ with respect to a decrease (short-term habituation) or increase of the variables concerned, within a session; the interaction between the factors environment and session indicates whether EC and IC animals differ with respect to an increase or decrease (long-term habituation) of these variables over sessions. As for the differential experience effects upon short-term habituation, it appears that the distance travelled (A), the number of shifts of position (D), as well as the behaviours W, R and S decrease significantly faster in EC animals than in IC animals. Whereas EC animals generally begin a session with a slightly higher level of locomotor activity than IC animals do, this locomotor activity decreases at a significantly higher rate over the second and third period in EC rats than it does in IC rats. Thus, EC rats show a faster short-term habituation than IC rats.The behavioural categories R and S demonstrate a similar effect of the environment within session. Behavioural category Z also reveals a significant environment*period interaction: the frequency of this behaviour increases significantly faster within a session in EC animals than in IC animals.
Measured over sessions (long-term habituation), EC and IC animals differ significantly with respect to distance

Table 4.1
Open field behaviour of EC and IC rats: distance travelled (A), number of shifts of position (D) and frequency of the various behavioural categories in each period for four consecutive sessions

		Session 1				Session 2				Session 3				Session 4				
		Period				Period				Period				Period				
		1	2	3	Tot	1	2	3	Tot	1	2	3	Tot	1	2	3	Tot	Total
A	EC	91	22	8	121	90	36	19	145	50	14	3	67	57	19	8	84	417
	IC	62	50	34	146	47	30	39	116	63	30	30	132	47	49	12	108	503
D	EC	24	6	3	33	24	10	5	39	14	4	1	19	14	5	2	21	112
	IC	25	20	12	57	14	9	11	34	17	11	8	36	12	12	3	27	154
W	EC	8	1	1	10	6	3	2	11	3	1	0	4	4	2	1	7	32
	IC	6	5	3	14	4	2	3	9	5	3	2	10	4	4	1	9	52
R	EC	4	2	1	7	5	2	1	8	4	1	0	5	4	1	0	5	25
	IC	3	3	2	8	2	2	2	6	4	2	2	8	3	3	1	7	29
O	EC	1	1	0	2	3	2	1	6	1	1	0	2	1	1	0	2	12
	IC	1	1	0	2	0	1	0	1	1	1	1	3	1	1	1	3	9
S	EC	20	10	5	35	18	9	8	35	17	7	3	27	17	5	3	25	118
	IC	18	13	10	41	15	8	7	30	15	8	5	28	15	5	3	23	122
T	EC	10	13	11	32	10	14	14	28	13	11	9	33	16	16	12	44	139
	IC	14	14	10	38	15	11	9	35	14	12	13	39	16	16	16	48	160
G	EC	2	2	2	6	3	3	0	6	2	2	1	5	2	2	1	5	22
	IC	3	5	3	11	3	2	1	6	3	4	3	10	3	2	1	6	33
P	EC	3	7	9	19	2	5	4	11	2	4	3	9	1	3	1	5	44
	IC	2	4	8	14	2	1	2	5	1	3	1	5	1	1	1	3	27
Z	EC	2	14	21	37	3	12	20	35	8	23	34	65	5	20	32	57	194
	IC	3	5	14	22	9	23	25	57	9	18	23	50	8	17	28	53	182

Table 4.2
Analyses of variance for the behavioural scores on the open field test (summarised in table 4.1)

	Env.	Session	Period	Env/ses	Env/per	Ses/per	E/S/P
	df 1,9	df 3,27	df 2,18	df 3,27	df 2,18	df 6,54	df 6,54
	F	F	F	F	F	F	F
A	1.525	2.098	28.166***	4.137**	10.274***	1.400	1.386
D	4.142	6.716**	29.586***	7.129**	7.296**	2.373*	1.306
W	6.719*	2.711	17.948***	3.430*	6.981**	2.316*	1.667
R	0.371	0.184	65.321***	2.258	7.903**	0.924	0.878
O	2.436	1.050	13.267***	4.877**	1.571	0.271	0.464
S	0.351	10.281***	141.609***	2.458	5.731*	1.469	0.208
T	0.198	2.625	3.846*	0.271	1.536	0.584	1.147
G	2.801	2.742	7.265**	1.466	0.382	0.654	0.954
P	3.068	13.736***	4.008*	0.212	1.112	4.001**	0.391
Z	0.240	6.094**	80.434***	4.674**	3.937*	1.035	0.568

* $p < .05$
** $p < .01$
*** $p < .001$

travelled (A), number of shifts of position (D), and frequencies of occurrence of the behavioural categories W, O and Z. The distance travelled (A), number of shifts of position (D) and walking (W) decrease from day 1 to day 2 and then stabilize in group IC, whereas for EC animals these variables decrease only from day 2 to day 3. In session 2 behavioural category O is scored more often for EC animals than for IC animals. The scores of category Z demonstrate a pattern that is opposite to that found for A, D and W: an increase from day 1 to day 2, and thereafter a relative stabilization are found in IC animals, whereas an increase in this variable from session 2 to session 3 is found in EC animals.

4.2.4. DISCUSSION

Animals reared in an impoverished environment behave differently in the open field from rats reared in an enriched environment. The above-reported experiment reveals that EC rats as well as IC rats begin a session in the open field with a comparatively high level of locomotor activity. In EC animals this locomotor activity decreases sharply over the 25 minutes of the session; this decrease is much less in IC animals. The same was found with respect to the behaviours R and S. Thus, IC animals demonstrated a slower functioning of the short-term habituation process. As a

result of this slower decrease of ambulation found in IC animals, the IC animals show significantly more ambulation (W) than EC animals when measured over the total 100 minutes observation time; they also more frequently shift their positions, the difference approaching significance here.
Determining whether EC or IC animals are the more active in the open field apparently depends upon the duration of the behavioural observations. Therefore, the results of research into potential differences in the total amount of locomotor activity of EC and IC animals in the open field, probably strongly depend upon the amount of time spent in the open field by EC and IC animals. If we had observed our animals in the open field for 8 minutes only, then on day 1 and day 2 EC animals would have been qualified as the more active group, whereas if we had kept them in the open field for an hour or so on the same days, the IC group probably had appeared to be more active. This way some of the often contradictory results with respect to locomotor activity of EC and IC animals may be explained, at least in part.
With respect to the rate of decrease of locomotor activity within session our expectations were confirmed: EC animals demonstrated a faster reduction in ambulation than their IC littermates. EC animals showed quicker behavioural changes. For the EC subjects the initially novel stimulus situation loses its relevance features sooner, which results in less locomotion, reflecting a more efficiently functioning stimulus selection in EC animals: the transition from relevance to irrelevance of a stimulus proceeds faster in the EC animals.
The differential experience effect on long-term habituation appears to be more complicated. Based on their results, several researchers (Whimbey and Denenberg 1967; Denenberg, 1969) formulated the assumption that the locomotor activity on the first test in the open field and that on subsequent tests is mediated by different processes. On the first day of testing ambulation would predominantly reflect escape behaviour, on the subsequent days it would reflect exploratory behaviour. Denenberg states that activity in the open field on the first test has an entirely different meaning from the activity on consecutive tests has (Denenberg, 1969, page 854). Aitken (1974) critisized this theory of Denenberg and showed that the calculations that lead to this theory were not performed correctly. So, interpretation of the effects upon long-term habituation as found here remains problematic. The environmental effects upon short-term and long-term habituation are not entirely comparable; this is in agreement with the suggestion of Rinaldi and Thompson (1985) that two different processes are involved.
Generally, it is found that in a forced exposure to the open field locomotor activity decreases. If, however, the animals are given the opportunity to enter the open field from a small adjacent cage, it appears that initially hardly any locomotion in the open field is observed at all; in that case locomotor activity increases over time (Welker, 1957; Aulich, 1976). Within the same stimulus situation, in the

first case a decrease in locomotion may be found and in the second case an increase.
As EC and IC animals differed with respect to the rate of decrease of locomotor activity, the question arose whether EC and IC animals would also differ with respect to the rate of increase of locomotion in an otherwise similar situation. This question will be examined in experiment 2.

4.3. EXPERIMENT 2. OPEN FIELD ACTIVITY OF EC AND IC RATS IN A FREE-ENTRANCE SITUATION

4.3.1. INTRODUCTION

Locomotor activity of the rat in an open field may be studied under two conditions. In the first condition the animal is forced to stay in the open field for a certain amount of time: he cannot escape from it. This condition was employed in the foregoing experiment 1. It is also possible to create a situation in which the animal can enter the open field from its own home cage and can also leave it again. This second condition will be used in the present experiment.
In a forced situation, as described in experiment 1, animals usually have a high initial activity that decreases as time proceeds. In a free-choice situation rats usually start with a few short visits to the open field from a small startbox (Welker, 1957; Aulich, 1976). Thus, in this situation locomotor activity in the open field is at a low level initially, but increases in the course of time. The stimulus situations in both conditions are equal. In the forced-exposure situation (experiment 1) EC animals exhibit a faster decrease of ambulation (within-session habituation) than IC animals do. In this experiment, it will be examined whether in a free-entrance situation EC and IC do differ also with respect to the usual increase in locomotor activity.
If their stimulus selection system did function less efficiently, we might expect that IC animals will be slower to differentiate between relevant and irrelevant stimuli in the new situation (Vossen, 1968; Warburton, 1972) and hence will respond less adequately. Gill et al. (1966) have already reported that IC rats took longer to enter the open field from an adjacent small cage, as compared with EC rats. Other publications concerned with learning experiments, sometimes reported that IC animals need more time to leave a startbox as compared with animals reared in a more enriched condition (Einon and Morgan, 1977), though once this difference was not found (Dalrymple-Alford and Benton, 1981a). The phenomenon might be explained by assuming that IC rats do habituate more slowly to the small startbox and thus show longer latencies. However, Lore and Levowitz (1966) found that IC rats also leave their homecage slower than EC rats. All these studies measured latencies of leaving the startbox. No studies have been done yet

examining the rate of increase of activity after the animal left the startbox.
Several researchers have demonstrated that a slower emergence as induced by exposure to IC environments, occurs independently from the age at which this exposure to IC environments had taken place (Einon and Morgan, 1977; Dalrymple-Alford and Benton, 1984). This is contrary to the effects upon rate of habituation, hyperactivity and reversal learning, which apparently depend upon an isolation time from weaning onwards and lasting from the age of 25 to 50 days (see Einon and Morgan, 1977; 1978b). This indicates that isolation immediately after weaning and isolation at a later age induce behavioral effects that probably possess different aetiologies.

4.3.2. METHODS

Subjects
In this experiment 20 male TMB rats served as subjects. 10 animals had been reared in an enriched environment, their 10 littermates in an impoverished environment. They had been weaned at approximately 25 days of age. Immediately after weaning they were placed in the respective environments, in which they lived for 30 days continuously. Thereafter they were housed individually in cages resembling the IC cages; these cages later on served as startboxes. Five days after termination of the differential rearing, the experimental procedure started (for a more extensive description of the pre-experimental procedure, see chapter 2).

Apparatus
The open field used here is almost identical with the one employed in experiment 1. The one change was a hole of 5x7 cms cut in one of the sidewalls. The open field was placed in the same experimental room as in experiment 1. Light was provided by a red bulb of 40 W placed 100 cms above the open field. As in experiment 1 observations were made from an adjacent room through a one-way screen.

Procedure
All rats were tested individually for 25 minutes (a session) per day on three consecutive days. Littermates were tested immediately after each other. The experimenter did not know from which environmental condition the individual animals came. All testing took place during the dark period of a 24-hours light/dark cycle. The procedure per session was as follows: the home cage containing the animal was placed against the hole in the sidewall of the open field. A sliding door closing off a corresponding hole in the home cage was removed and one minute later behavioural observations started. Locomotor activity was recorded the same way as in experiment 1 (4.2.3). Moreover, the latency of the first emergence from the home cage into the open field was recorded also; a distinction was made as to two forelegs of the animal leaving its homecage (a) and the entire body leaving the homecage (b).

4.3.3. RESULTS

In this situation in which the animal could enter the open field from its home cage through a small opening, EC as well as IC animals hardly left their home cages during the three sessions of 25 minutes each. Scoring the frequencies of the various behavioural categories proved futile, since only six animals from the EC condition as compared with none of the IC group left their home cages at last.
This experiment, therefore, demonstrates that if animals can enter the open field from their own home cages, they will do so only after a certain amount of time has elapsed. The beginning of any activity developed so slowly in this experiment, that the expected increase in activity followed by an expected decrease in both experimental groups could not be measured. The latency values (Table 4.3) indicate that EC rats were inclined to enter the open field from their home cage sooner than IC rats did, with two forelegs as well as with the entire body. It appears that the start of activity for EC animals differs from that for IC animals: EC animals start earlier from their home cage with a little activity in the open field than IC animals do.

Table 4.3
Mean latency in seconds of leaving the home cage with a) two frontlegs and b) the total body, and the number of animals per condition which showed that behaviour, for EC and IC rats.

		Session 1		Session 2		Session 3	
		$\bar{X}$	number	$\bar{X}$	number	$\bar{X}$	number
Latency-	EC	220	9	137	9	133	9
2 fore feet	IC	600	5	612	5	528	5
Latency-	EC	610	3	222	5	315	6
total body	IC	-	0	-	0	-	0

4.3.4. DISCUSSION

Our observations indicate that the very slow starting of visits to the open field might have been caused partly by the manner in which the animal had to leave its home cage in order to enter the open field. The animals were observed

holding their heads continuously before the hole in the open field and many rats threw woodshavings from their homecages through the hole into the open field. One got the impression that this situation was very frightening for the rats. Blanchard et al. (1974) found something comparable with this. They also observed that a free-entrance situation as ours evoked a number of responses that closely resembled those evoked by frightening stimuli. They also found that rats that were in the open field for the first time, would escape to their home cages even though they received a moderate shock in front of the entrance to their home cages. On the other hand, a very low-intensity shock received upon entering the open field from the home cage, sufficed to leave the open field entirely unused (Blanchard et al., 1974).
It was decided to develop a situation in which the transition from home cage to open field would be realized differently. This different method of contact between home cage and open field is not confined to a small spot, but takes up a larger space. This might result in the animals leaving their home cages sooner than they did in experiment 2. If so, we would be able to measure the influences of rearing environment upon changes in locomotor activity in an open field, employing a free-entrance situation.

4.4. EXPERIMENT 3. OPEN FIELD ACTIVITY OF EC AND IC ANIMALS IN A FREE-ENTRANCE SITUATION: A MODIFICATION

4.4.1. METHODS

Subjects
Subjects were 20 male TMB rats, 10 having been reared in an enriched environment cage, their 10 littermates having been reared in IC cages. All animals were weaned at an age of 25 days and immediately thereafter placed in their respective environments in which they remained for 30 days continuously. Subsequently, all subjects were housed individually in IC-type cages that were to serve as startboxes later on in the experiment. Five days after rehousing the experimental procedure started.

Apparatus
The open field, measuring 50*50*15 cms, was made of wood and painted light grey. One of the sidewalls was provided with a mirror at the inside; the opposite wall and the cover were made of plexiglass. In the center of the floor of the open field a hole of 37*25 cms was cut in which the upper rim of the macrolon cages fitted precisely. The open field was placed upon four legs, in such a way that the upper rim of the home cage was exactly level with the floor of the open field. The open field was located in a separate experimental room. This room was illuminated by a red bulb of 40 W, placed 100 cms above the open field. Behavioural observations were made as usual through a one-way screen.

Procedure
All rats were tested individually for 25 minutes per day (a session) on three consecutive days. Littermates were tested one immediately after the other. A session proceeded as follows: the home cage containing the rat was placed below the hole in the floor of the open field, in such a way that its upper rim connected smoothly with the floor of the open field. Through climbing out of its home cage the animal could enter the open field. Behaviour was recorded continuously. Behaviours registered were:
- time elapsed until the rat left the home cage for the first time with his whole body (latency);
- number of visits to the open field;
- duration of individual visits to the open field;
- total amount of time spent in the open field per session.

4.4.2. RESULTS

Table 4.4 shows the mean latencies, the mean number of visits and the mean total time spent in the open field per session for the EC and IC groups respectively. An analysis of variance (table 4.5) reveals that EC rats visited the open field more often than IC rats did and spent a significantly larger part of the total observation time of 75 minutes in the open field. The total time in the open field and the number of visits changed over days: EC animals as well as IC animals showed increasing values for these variables. However, these changes did not develop differently for EC and IC animals respectively. Concerning latency, it was found that EC rats showed shorter latency times on session 1 and session 2 (Sign test, $p<.01$). No difference was found on session 3.

4.4.3. DISCUSSION

In this experiment again, EC as well as IC animals start with a low level of locomotor activity in the open field. As in experiment 2, the IC rats develop locomotor activity significantly later than EC animals do. This agrees with reports of Gill et al. (1966), Lore and Levowitz (1966), Einon and Morgan (1977) and Dalrymple-Alford and Benton (1984). As time proceeds, locomotor activity increases in both groups. However, a difference between groups in the rate of increase, as measured over sessions, was not found. EC as well as IC animals pay comparatively short visits to the open field. Mean duration per visit does not reveal group differences either, though increases over days are found in both groups. Thus, enlarging the area of contact between start/home cage and open field did have an effect in that the open field was entered sooner; even so, both EC and IC animals entered the open field with much hesitation.
Einon and Tye (1975) explain the differences in emergence time between EC and IC animals they had found (e.g. Einon and Morgan, 1977) in terms of IC animals being more timid than EC animals. The difference in emergence time could be

Table 4.4
Mean latency time in seconds of leaving the home-cage, mean total time out of the home-cage and the mean number of visits to the exploration box for EC and IC rats in three consecutive sessions

		Session 1		Session 2		Session 3	
Latency time	EC	154.3	n=10	84.9	n=10	127.9	n=10
	IC	567.5	n=4	408.8	n=4	355.0	n=7
Total time	EC	72.1		96.4		177.0	
	IC	4.6		16.7		48.1	
Number visits	EC	22.0		12.3		26.7	
	IC	1.4		4.2		7.5	

Table 4.5
Analyses of variance for the behavioural scores on the open field test (summarised in table 4.4, excluded the mean latency time)

	Env.	Session	Env/ses
	df	df	df
	1,9	2,18	2,18
	F	F	F
Total time	9.386 *	8.326 **	1.484
Number visits	14.005 **	4.301 *	2.286

*$p < .05$ **$p < .01$

abolished by *administering chlorpromazine* (a major tranquilizer) to the IC rats. However, data reported by Dalrymple-Alford and Benton (1981a) render it less plausible that the behavioural differences between EC and IC subjects found there, reflect a difference in fear/emotionality: it was found that during a forced exposure to the open field IC rats do not walk along the walls of the open field any more than do EC animals (Dalrymple-Alford and Benton, 1981a).

4.5. EXPERIMENT 4. EFFECTS OF DIFFERENTIAL EXPERIENCE IN ENRICHED AND IMPOVERISHED ENVIRONMENTS ON HABITUATION OF THE ACOUSTIC STARTLE RESPONSE

4.5.1. INTRODUCTION

Habituation can be measured by recording decreases in locomotor activity in the open field (experiment 1), and also through measuring the rate of decrement of the startle response to aversive acoustic stimuli. It has been found that cholinolytica such as scopolamine induce a reduction of locomotor acitivity in the open field, but do not affect the rate of attenuation of startle response (Williams et al., 1974). If EC and IC animals had differently functioning cholinergic systems, one might assume that EC and IC animals will differ with respect to the rate of decrease of locomotor activity in the open field (as found in experiment 1). However, a difference in the rate of attenuation of the startle response to aversive acoustic stimuli is not to be expected, unless other neural systems, that are essential for the habituation of startle responses, function differently in EC and IC animals also.

4.5.2. METHODS

Subjects
In this experiment 20 male TMB rats were used: 10 animals had been reared in an EC environment for 35 days, their 10 littermates had been reared in an IC environment from weaning around day 25 onwards. For an extensive description of the preexperimental procedure, see chapter 2. At the time of testing the animals were approximately 63 days of age.

Apparatus
The animals were tested in a small cage of 15*8*8 cms. The top and frontwall were made of plexiglass and contained a few air holes. All other walls were made of aluminium. The cage was mounted upon a hard rubber base, 5 mms thick. A phonograph cartridge rested on the top of the cage. Cage movements caused by the rat were monitored by the cartridge crystal. The resulting changes in voltage were fed into an amplifier and sent through a low-pass filter, to prevent registration of oscilliations caused by the acousttic stimulus itself. Finally, the voltage output was fed into an UV recorder (S.E. 3006) that recorded the voltage changes graphically.
Two seconds before presentation of the startle stimulus the UV recorder was triggered and ran for 4 seconds with a paper speed of 50 cms/min. Startle amplitude was determined by measuring the trace amplitude to the nearest mms and converting this value to millivolts.
Startle stimuli resembled those of Davis (1972). With an interstimulus interval of 30 seconds tone stimuli of 4000 Hz were presented during 0.1 second; the intensity of each tone was 102 dB, measured inside the cage.

Procedure
On the first day of testing (day 1) the animal was placed in the startle cage. After 10 minutes the first startle stimulus was presented. The whole session consisted of 40 presentations of the tone stimulus with an interstimulus interval of 30 seconds. After the session the animal was removed from the experimental cage and returned to its home cage. The order of testing the EC and IC animals was determined so as to balance diurnal rhythm effects. The experimenter was not aware of which animal came from which condition. This procedure was repeated on the second day (day 2), the eighth day (day 3) and the ninth day (day 4).

4.5.3. RESULTS

For individual animals the mean startle amplitudes of successive blocks of five trials were calculated (Davis, 1972). Thus, for days 1, 2, 3 and 4 eight block scores each were obtained. In figures 4.1 to 4.4 the mean block scores and their standard errors are depicted for the groups EC and IC on day 1, 2, 3 and 4.
The data of the startle responses were tested by trend analyses with the factors environments, days and litters. Amplitude decrement per day was mainly determined by a linear trend (explaining 65% of the variance), a quadratic trend (21% of the variance) and a cubic trend (11% of the variance). As to these trends (short-term habituation) neither an effect of environment, nor a difference between days, nor an interaction between both was found. Over days (long-term habituation) an attenuation of the startle response was found ($F(3,27) = 5.80$; $p<.01$). In this respect EC and IC animals did not significantly differ.

4.5.4. DISCUSSION

It is clear that EC as well as IC animals showed a decreasing amplitude of startle responses. The rate of decrease, however, did not differ in both groups. The occurrence of a difference in rate of habituation between EC and IC animals, as measured through locomotor activity in the open field, combined with the absence of a difference in rate of habituation between EC and IC animals, as measured through the amplitude of startle responses to intense acoustic stimuli (experiment 4), supports the assumption that these two habituation processes cannot be ascribed to one and the same physiological process (Williams et al., 1974).
Exploration presupposes the execution of behaviour that leads to response-contingent feedback. This feedback reduces the relevance of the novel stimulus; the stimulus loses its novelty features. The integration of feedback functions as reinforcement, but also causes feedback that does not add any new information to lose its reinforcing power: exploratory behaviour will then be inhibited. Such processes are sensitive to cholinergic influences. Attenuation of the

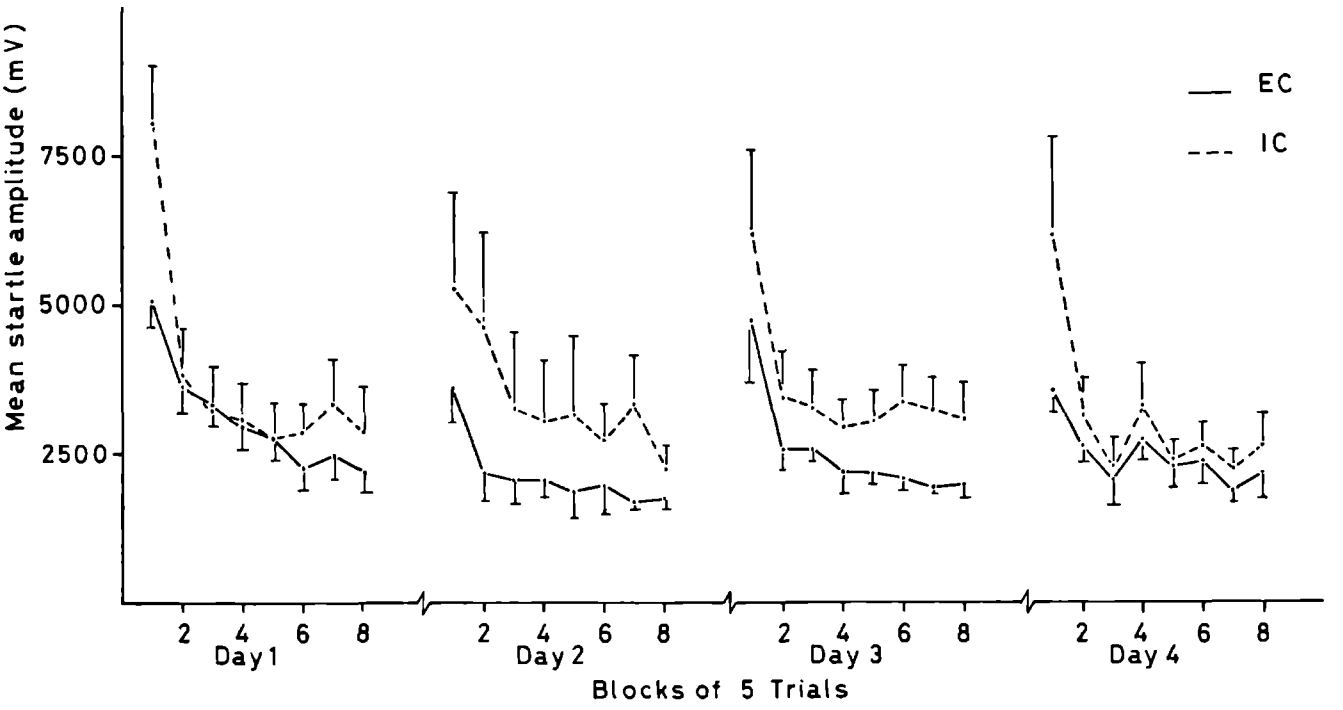

Figure 4.1. Mean block scores of startle amplitude and SEM's of EC and IC rats on days 1, 2, 3 and 4.

startle response does not depend upon response-contingent feedback. The differences in habituation between EC and IC animals thus appear to be determined by a less effective integration of response-contingent feedback in IC animals: the stimulus-selection process of these animals functions less efficiently, which has a negative influence upon relevant stimulation becoming irrelevant.

CHAPTER 5

EFFECTS OF DIFFERENTIAL EXPERIENCE IN ENRICHED (EC) AND IMPOVERISHED (IC) ENVIRONMENTS ON DISCRIMINATION AND REVERSAL LEARNING

5.1. INTRODUCTION

Discrimination and reversal learning can be considered behavioural processes in which efficiency of stimulus selection, particularly the inhibition of irrelevant stimuli, plays an important role. This becomes apparent from such phenomena as the overtraining reversal effect (ORE), overshadowing and blocking (Sutherland and Mackintosh, 1971). Descriptions of these stimulus selection processes are summarized in a theory and formalized in a model with the main theme being selective attention (Mackintosh, 1973, 1975). According to this theory, the rate of discrimination learning, the learning about a stimulus, depends on the amount of attention given to the stimulus. In his model, Mackintosh introduces a stimulus-specific learning rate parameter α. α represents the associative strength of the stimulus: the higher α is, the more associative strength there will be and the easier learning about that stimulus will proceed. The value of is determined not only by the physical properties of the stimulus and the qualities of the sensory apparatus of the organism, but changes by experience as well. If stimulus A is correlated with reinforcement changes, αA will increase, if stimulus B is not correlated with reinforcement changes, αB will decrease. Thus, animals learn to pay attention to relevant stimuli and to ignore irrelevant stimuli. The heigth of the α-value of a stimulus will generally increase and decrease dependent on that stimulus'correlation with reinforcement. On page 17 we formulated the hypothesis that EC and IC animals differ as to efficiency of stimulus selection, particularly the inhibitory efficiency towards irrelevant stimuli. Applying Mackintosh's theory to this hypothesis, we would expect that EC and IC animals will differ particularly with respect to the decrease of the α-value of those (irrelevant) stimuli that are not correlated with reinforcement.

5.2. EXPERIMENT 1. EFFECTS OF DIFFERENTIAL EXPERIENCE IN ENRICHED (EC) AND IMPOVERISHED (IC) ENVIRONMENTS ON BRIGHTNESS DISCRIMINATION AND REVERSAL LEARNING

5.2.1. INTRODUCTION

One of the first experiments published by the Berkeley group, concerning the effects of rearing in environments of varying stimulus complexities on behaviour, reports that EC and IC animals do not differ as to the learning of a

brightness discrimination, although at subsequent reversals of the problem EC animals showed significantly fewer errors than IC animals (Krech et al., 1962). Differences in reversal learning in different learning situations were reported by Collins (1970) and Morgan (1973). A characteristic feature of reversal learning is that the relevance features of stimuli change: a stimulus or stimulus configuration changes from relevant into irrelevant, whereas another stimulus or stimulus configuration changes from irrelevant into relevant. An efficiently functioning stimulus selection system promotes adequate reversal learning.
In the first instance, we will try to replicate the Berkeley findings. Therefore, we will use a maze and learning procedure that are identical with those employed by the Berkeley group. Hence, we expect that EC and IC animals will not differ in the learning of the brightness discrimination problem in a multiple-unit discrimination box, and that after reversals of the problem EC animals will demonstrate better learning performance than their IC littermates do.

5.2.2. METHODS

Subjects

In this experiment 10 subjects were used: five littermate pairs of male TMB rats. Five animals were reared in an EC condition, the other five in an impoverished condition. After weaning at approximately 24 days of age, these animals were reared in their respective environments for 40 days. A description of the environments as well as a description of the group assignment procedure and the living conditions in both environments, are presented in chapter 2. After termination of the differential rearing all subjects were rehoused individually in macrolon cages of the standard condition type. Three days later individual behaviour tests started.

Apparatus

During pre-training a runway was used measuring 12x11x16 cms and made of Masonite (fig. 5.1). The top of the runway was covered with a plexiglass sheet. The start compartment could be closed off from the remainder of the runway by a sliding door of masonite. The behaviour of the animal in the runway could be observed through mirrors.
In the discrimination and reversal learning tasks Krechevsky's Multiple-unit Discrimination Box (KMDB, also called Krech Hypothesis Apparatus, KHA) was used. This multiple-unit discrimination box is essentially a linear maze containing four successive Y-shaped choice points (fig 5.2). This maze measured 191x26x14 cms and was constructed of wood. The top was made of plexiglas and observations were made through mirrors. Above each alley in each unit 15W bulbs were placed, so that each alley could be lit separately.

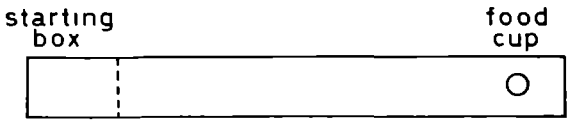

Figure 5.1. Floor plan of the pre-training runway.

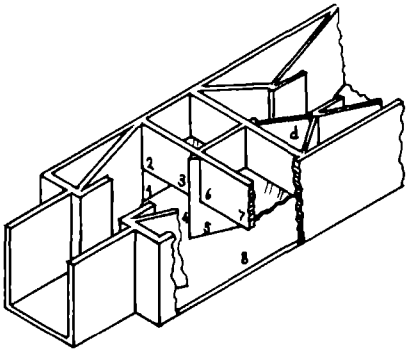

Figure 5.2. Floor plan and elevation of Krechevsky's multiple-unit discrimination box. The door d can swing so as to block either alley 1-4 or 5-8. Above each alley in each unit (in chambres 2-3 and 6-7) are electric lamps that can flood either alley with light. (After Krechevsky, 1932a).

Procedure

Pre-training

Pre-training started three days after termination of the differential housing. 36 hours before the first pre-training trial subjects were placed on a food deprivation schedule. The first 36 hours of the schedule they did not receive any food. Subsequently, they received 12 grams of food

immediately after each training session. Water was available ad libitum. The animal's weight was thus reduced to 90% of its normal weight, taking into account the normal weight increases in animals of this age. Pre-training lasted a total of ten days. On the first three days the animal was allowed to freely explore the runway during 5 minutes a day; five Noyes food pellets were placed in the food tray. On day 4 to day 10 each animal received three successive trials a day. A trial proceeded as follows: the animal was placed in the start-box, the slide was removed and the recording of time started. The time recording stopped again as soon as the animal started eating. Then, the animal was removed from the runway, the runway was cleaned and the next trial started. In each trial three Noyes pellets were placed in the food tray. Two days after termination of the pre-training, the discrimination learning in the Krechevsky Multiple-Unit Discrimination box (KMBD) was started.

Discrimination and reversal learning

The learning procedure employed in the discrimination learning and reversal tasks was similar to that of the Berkeley group (Bennett et al., 1970). Each rat received 10 successive trials per day and thus had to make 40 choices a day.

The first learning task involved a light-dark discrimination. During the initial learning (OL) of the brightness discrimination the lit alley represented the correct choice. An error was scored when the animal had crossed a line at the beginning of the incorrect alley (during OL the unlit alley) with both its frontlegs. At that point the rat was not yet able to see that the "wrong" alley was closed. Each trial, containing four choice points, the light-dark pattern was changed. The animal was considered to have learned the problem if it made one error at the most in five successive trials. Thus, the learning criterion was met if 19 of 20 successive choices were correct.

Immediately after reaching criterion reversal learning (R) started. The start of this reversal learning might occur any time during a daily session of 10 trials. During the first reversal (R1) the dark alley was the correct alternative. Reversal learning on task R1 was terminated if again the criterion of 19 correct choices during 5 successive trials was reached. Immediately thereafter, a new reversal task (R2) was started, the lit alley being the correct choice again. Each animal learned a total of four reversals (intra dimensional shifts).

5.2.3. RESULTS

Pre-training

The mean latency per trial on day 4 to 10 is presented in figure 5.3. From this graph it can be seen that IC animals score longer latencies than their EC littermates do. An analysis of variance demonstrated a significant effect of environment with respect to runway times on each day of training. The differences between EC and IC animals become

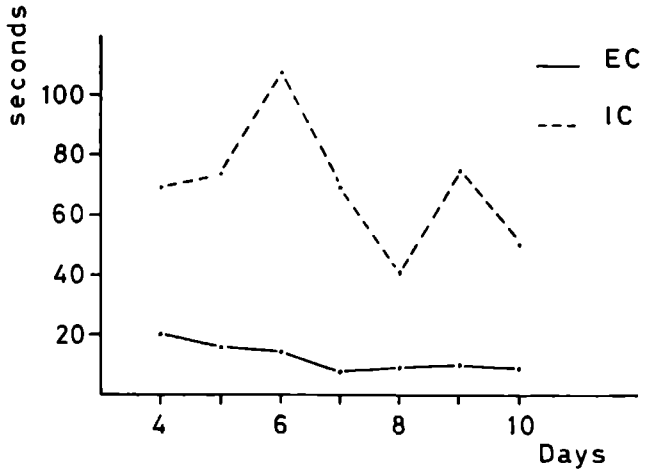

Figure 5.3. Mean latency (in seconds) a day for EC and IC rats during pre-training.

smaller, however, as pre-training days proceed; nevertheless the differences remain at a significant level from day 4 ($F(1,4)=7.87$; $p<.05$) to day 10 ($F(1,4)=8.15$; $p<.05$).

Discrimination and reversal learning

Figure 5.4 depicts the mean number of errors made by EC and IC animals during the OL, R1, R2, R3 and R4 tasks respectively. Analyses of variance performed on the number of errors reveal that a difference between EC and IC animals is found only at the first reversal task (R1). EC animals make significantly less errors than IC rats ($F(1,4)=10.535$; $p<.05$). The differences during the initial learning and the third reversal (R3) almost reach significance (OL: $F(1,4)=3.18$; $p<.11$ and R3: $F(1,4)=4.14$; $p<.08$).

Figure 5.5 shows the number of trials needed to reach the learning criterion. Analyses of variance over the number of trials reveal that EC rats needed fewer trials than IC rats, not only during R1 ($F(1,4)=13.991$; $p<.01$) but also during the original learning ($F(1,4)=6.496$; $p<.05$), R3 ($F(1,4)=7.162$; $p<.05$) as well as R4 ($F(1,4)=7.942$; $p<.05$).

5.2.4. DISCUSSION

Already during pre-training a behavioural difference between EC and IC reared animals becomes apparent. EC animals run through the alley much faster than IC animals do. The same was observed by Greenough et al. (1972). These results indicate that initially freezing behaviour occurs more frequently in IC animals, as was found in the experiments 2 and 3 of chapter 4 also. During the original learning of the

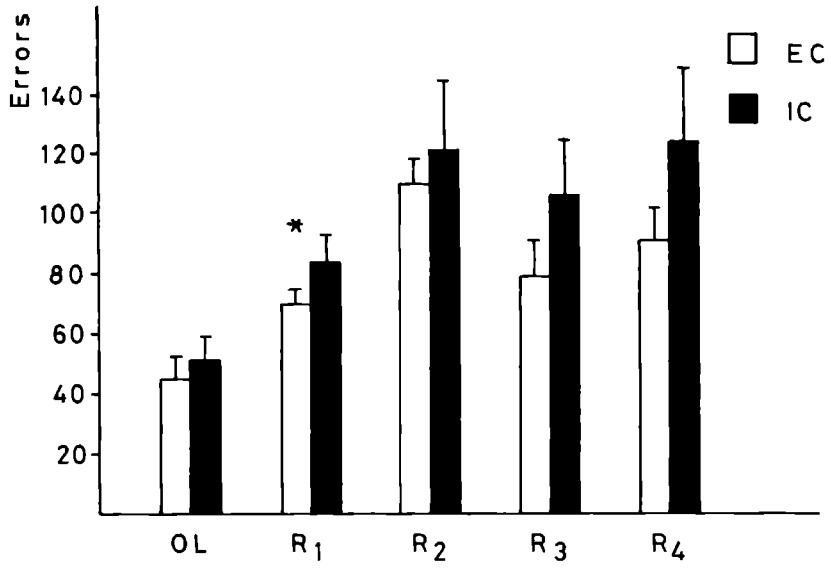

Figure 5.4. Mean number of errors (± SEM) for EC and IC rats on the acquisition of a visual discrimination problem (OL) and on subsequent visual reversal problems (R1, R2, R3 and R4: intradimensional shifts).

*p < 05

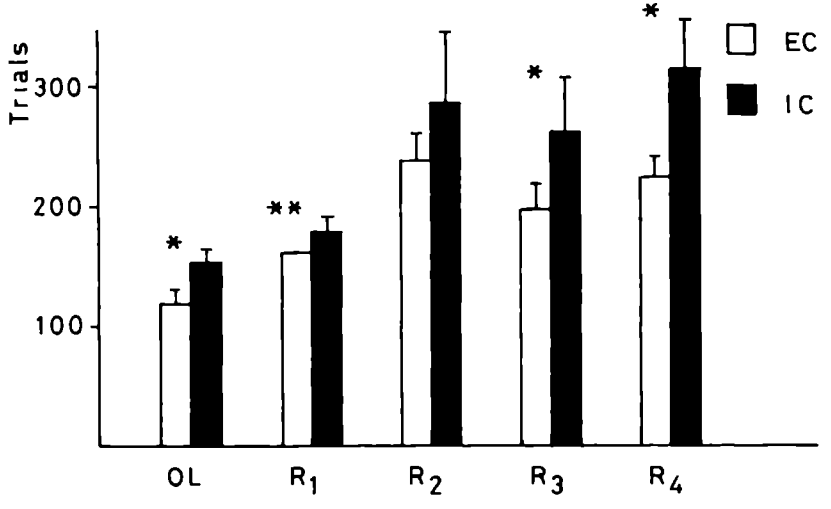

Figure 5.5. Mean number of trials (± SEM) for EC and IC rats on the acquisition of a visual discrimination problem (OL) and on subsequent visual reversal problems (R1, R2, R3 and R4: intradimensional shifts).

*p < 05 **p < 01

brightness discrimination in the KMDB EC and IC animals do not differ as to the number of errors made before reaching criterion. During the first reversal of the problem EC animals make significantly fewer errors than IC animals do. Thus far our results replicate the data published by Krech et al. (1962). However, in Krech's results the difference between EC and IC animals remains significant in the subsequent reversals, whereas in our experiment no differences in number of errors are found in R2, R3 and R4. If we consider the number of trials, however, it is clear that EC animals need less trials to reach the learning criterion than IC animals do, during R1 as well as during OL, and R3 and R4. The fact that during OL a significant difference in the number of trials needed has been found, probably indicates that during OL there is already a difference in learning behaviour.

Let us closely consider the learning and reversal learning of the brightness discrimination.

According to Krechevsky (1932), in an experimental situation such as the KMDB animals do not just respond to the stimuli presented, but they develop some kind of hypothesis as to which stimuli are of relevance and which are not. After some time, in consequence of reinforcement not always occurring, the animals will replace their nonsuccessful hypotheses and try other new ones. How these hypotheses are substituted, according to which rules, Krechevsky did not clearly describe, in that he merely talked about "new insights". However, Mackintosh's theory (1973, 1975) on selective attention, stimulus selection processes and associative strenghts of stimuli offers good opportinities to describe the mechanisms of establishing, maintaining and replacing the hypotheses.

During the learning of the brightness discrimination in the KMDB animals might initially select responses either on the basis of a left-right distinction (spatial discrimination hypothesis) or on the basis of a light-dark distinction (brightness discrimination hypothesis). Experiments published by Krech et al. (1954) have demonstrated that TMB rats have a preference for spatial hypotheses in the KMDB. One might assume, then, that TMB rats in first instance will start to test a spatial hypothesis and only later on shift to testing a visual hypothesis. In fact, that would mean that during the learning of the problem the animals actually go through an extradimensional shift (EDS). During the first learning a number of discriminative stimuli are present: spatial stimuli (left-right) and brightness stimuli (light-dark) to which the rat can respond. Each of these stimuli has a certain associative strength: α. If associations with the light stimulus are to be learned, the α-value of this stimulus has to gain strength, whereas the α-values of the remaining stimuli (dark, left and right) have to decrease. If the latter values remain too high, the animal will keep responding to these stimuli occasionally. The tendency to pay attention to a stimulus depends entirely upon the α-value of that stimulus. However, an increase in the α-value of a certain (say: relevant) stimulus does not automatically imply a decrease in the α-values of other

stimuli: decreases and increases of the α-values of these other stimuli depend exclusively upon these stimuli being correlated or not with reinforcement (Mackintosh, 1975). Consequently, during the first reversal the animals have to extinguish their hypothesis based upon visual stimuli. Subsequently, in view of their preference, they might first try a spatial hypothesis again before finally developing a new visual hypothesis. In other words: during reversal learning the α-value of light (which has increased during the initial learning of the brightness discrimination) has to be reduced to a low value, whereas at the same time the α-value of dark (which during the initial learning has become quite low) has to increase again. The α-values of left-right have to remain low. To examine this process closer, the results have been put through a more detailed analysis.

For each series of four consecutive trials it was determined how often each animal made a choice to the left, to the right, to the light or to the dark. In four trials an animal had to make 16 choices: if 13 or more of these choices were towards one of the cues mentioned, it was assumed that the animal had a hypothesis about that cue: thus, it could be determined whether light, dark, left and right hypotheses were employed, how long these were maintained and whether there were any periods without hypotheses and if so how many and how long these lasted. The differences between EC and IC animals were tested through nonparametric tests. The analyses revealed that EC and IC animals differed in the number of spatial hypotheses employed during the entire training period (OL to R4). IC animals employed significantly more spatial hypotheses than EC animals did. The difference is particularly clear during the latter reversals (R3 and R4). Responding mainly on the basis of spatial hypothesis leads to an increase in the number of trials needed to reach criterion. The effect on the number of errors is less outspoken: if a spatial hypothesis is used (for example, to the right) 50% of the choices is correctly made. This explains why EC and IC animals differ in number of trials to criterion but not in number of errors made. When we consider the behaviour of EC and IC animals in terms of the theory of Mackintosh, it appears that the α-values of irrelevant place-stimuli (left-right) are not as low in the IC animals as they are in the EC animals, particularly so with an increasing number of reversals. This indicates that in IC animals the attention for these irrelevant stimuli is not suppressed as well as it is in EC animals. If a subject selects a choice between left and right and light and dark, place stimuli are 50% reinforced and 50% nonreinforced. If IC animals are less efficient in inhibiting irrelevant stimuli, that is, if they show a slighter decrease in the α-value due to non-reinforcement, then in due time the α-values for place stimuli will become larger for IC animals than they are for EC animals. On the other hand, there is the possibility that IC animals show a larger increase in α-value due to reinforcement than EC animals do. However, in that case one would expect that IC animals would reach criterion faster than EC animals.

Contrary to our expectations, TMB rats did not initially develop a left or right hypothesis: a spatial hypothesis as the first hypothesis employed was found in only one (IC) animal. During reversal training, after they had learned a light or dark hypothesis, the TMB rats almost always developed a spatial hypothesis first. Based on the findings of Krech et al. (1954) that TMB rats have a preference for spatial stimuli, in contrast with TMD rats that have a preference for brightness stimuli, it seems plausible that in TMB rats, the α-values of place stimuli are higher than the α-values for brightness stimuli, which maybe is genetically determined. Another result of the closer analysis is that only during the first reversal IC animals keep responding longer to the learned cue of the initial task (light) and thus maintain a light hypothesis longer than EC animals do. Thus, at the beginning of the R1 IC animals stick to their hypothesis: light=correct longer. All responses to this cue are incorrect. This might have played an important role in the occurrence of a significant difference in number of errors between EC and IC animals during the first reversal. Initially, IC animals apparently have more difficulties in inhibiting α-values that have risen high. Later on, during subsequent reversals, their capacity for inhibition does not appear to differ anymore from that of EC animals. All other variables examined (time to occurrence of first hypothesis, time to correct hypothesis, duration of incorrect hypothesis, duration of period without any hypothesis) did not reveal any differences between EC and IC animals.

In this experiment two stimulus dimensions were involved in the test situation: a spatial and a brightness dimension. It seems that the differences between EC and IC animals are caused by the IC animals being hindered by the irrelevant stimulus dimension more than the EC animals are. IC animals apparently are less capable to lower the α-values of these irrelevant stimuli. Moreover, there is some evidence that within the relevant brightness stimulus dimension IC animals initially have difficulties with inhibiting the stimulus that gained relevance in the task learned before. Finally, the behaviour of the animals lead to the assumption that the α-values for place stimuli might be higher than those for brightness stimuli in this strain of rats, which might be genetically determined. The employment of spatial hypotheses and the presence of an irrelevant stimulus dimension (location) apparently play important roles in the occurrence of differences between EC and IC animals in learning behaviour in a visual discrimination problem.
Hence, it might be useful to carry out an experiment in the KMDB that does employ only one stimulus dimension. Thus, the animals were exposed to a discrimination task that can be solved at once on the basis of a spatial hypothesis and does not allow for the development of visual hypotheses. This procedure will be described in experiment 2.

5.3. EXPERIMENT 2. EFFECTS OF DIFFERENTIAL EXPERIENCE IN ENRICHED (EC) AND IMPOVERISHED (IC) ENVIRONMENTS ON SPATIAL DISCRIMINATION LEARNING AND ON REVERSAL LEARNING WITH INTRA- AND EXTRADIMENSIONAL SHIFTS

5.3.1. INTRODUCTION

In this experiment EC and IC subjects will be exposed to spatial discrimination and reversal learning tasks in the KMDB. During the replication experiment, experiment 1, the subject had a choice between two stimulus dimensions (spatial and brightness dimension) to solve the learning problem. In this experiment, the learning behaviour will be examined employing one dimension only, the spatial dimension. In view of the fact that TMB rats prefer spatial hypotheses over visual hypotheses (Krech et al., 1954; see also Vossen, 1966), we expect that TMB rats will learn the spatial discrimination faster than they learned the visual discrimination of experiment 1. Moreover, we will examine whether in a situation that allows for choices within one dimension only, IC and EC animals will differ with respect to the initial learning of the spatial discrimination. We certainly expect a difference during the first reversal: as in experiment 1, we expect that IC animals will keep responding longer to the initially relevant stimulus, and that the difference will disappear during subsequent reversals. In the last reversal (R4) an extradimensional shift (EDS) will be introduced. Instead of a spatial discrimination, the animals will be confronted with a visual problem, as in experiment 1, during which spatial stimuli are irrelevant again. The expectation is that EC and IC animals will differ in learning behaviour, since in this situation again several irrelevant stimuli are present.

5.3.2. METHODS

Subjects
20 Male TMB rats served as subjects: 10 animals reared in an enriched condition and 10 rats reared in an impoverished condition. The animals remained in their respective environments during 30 days, from weaning at an age of 25 days onwards. A description of the environments used, the method of group assignment and the housing conditions has been given in chapter 2. After termination of the differential rearing all rats were rehoused individually in macrolon cages of the IC type. Three days later individual testing began.

Apparatus
During pre-training the same runway was used as in experiment 1 (5.2.2, figure 5.1). For the discrimination and reversal learning, the Krechevsky multiple-unit discrimination box (KMBD) was used again (5.2.2, figure 5.2). Since this experiment aimed at examining the learning of spatial discrimination tasks from OL to R3, each alley in

the KMBD was illuminated. During the fourth reversal in which the animals had to learn a brightness discrimination, illumination was similar to the situation during the OL-phase of experiment 1.

Procedure
Pre-training started three days after termination of the differential housing. Food-deprivation and pre-training proceeded the same way as in experiment 1 (5.2.2). Two days after completion of the pre-training the learning of the spatial discrimination started. Animals were confronted with a total of five discriminative problems. Each problem had to be learned within one session, upon one and the same day; this contrasts with the procedure followed in the first experiment. The learning programme comprised a total of five days. Thus, each day started with a novel problem to be learned and the animal was trained until the learning criterion was reached. The learning criterion again was 19 correct choices out of 20 successive choices, made in consecutive trials. On the first four days the animals were exposed to spatial discriminations (OL, R1, R2, R3). On the fifth day a brightness discrimination was presented (extra dimensional shift). The illuminated alley represented the correct choice here.

5.3.3. RESULTS

Pre-training
Mean latencies per trial on day 4 to 10 are presented in figure 5.6. Analyses of variance performed on these data

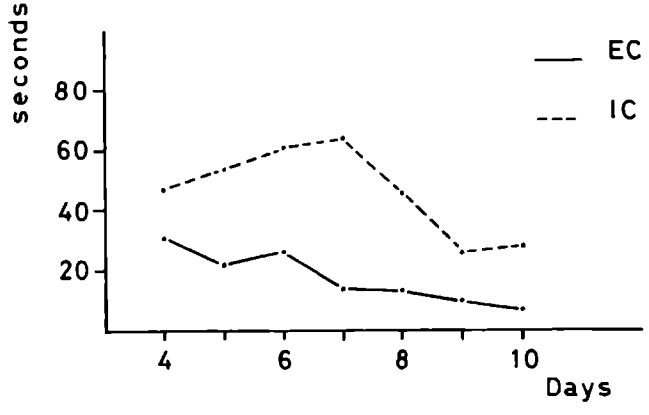

Figure 5.6. Mean latency (in seconds) a day for EC and IC rats during pre-training.

revealed that EC animals have shorter latencies than IC animals have. From day 5 to 10 these differences are significant, on the first pre-training day they were not (day 5: $F(1,9)=21.20$; $p<.01$; day 10: $F(1,9)=15.32$; $p<.01$).

Discrimination and reversal learning

Figure 5.7 depicts the mean number of errors made by EC and IC subjects during OL, R1, R2, R3 and the extradimensional shift, R4. Analyses of variance revealed that EC animals made significantly fewer errors during the first reversal ($F(1,9)=8.373$; $p<.05$)) as well as during the extradimensional shift R4 ($F(1,8)=13.558$; $p<.01$).

Figure 5.8 shows the mean number of trials needed by EC and IC animals on OL, R1, R2, R3 and R4.

Analyses of variance demonstrated that as far as the number of trials needed is concerned, no differences between groups exist. During the extradimensional shift (R4) the difference between EC and IC animals approaches significance ($F(1,8)=3.656$; $p<.10$).

5.3.4. DISCUSSION

Just as in experiment 1, we found that EC animals have shorter running times than IC animals during pre-training in the runway. If we compare the learning performance of EC and IC animals in this experiment with those observed in the first experiment, then it appears that EC as well IC animals learn a spatial discrimination much faster than a visual discrimination, which is as expected. During the acquisition of the visual discrimination EC and IC animals made 46 and 51 errors respectively, whereas during the mastering of the spatial discrimination problem only 12 and 13 errors respectively were made. This difference in learning rate between the learning of a brightness discrimination in experiment 1 and a spatial discrimination in experiment 2 might be caused by a (genetically determined) higher α-value of spatial stimuli than of brightness stimuli in TMB rats, which predisposes these animals to learn these cues faster. On the other hand, the amount of irrelevant stimulation (which was larger in experiment 1 than in experiment 2) might have played an important part.

In this experiment, no differences betweeen EC and IC animals in the learning of a spatial discrimination were found, as far as number of errors and number of trials needed is concerned. Thus, the learning of a spatial discrimination in the absence of additional irrelevant stimulus dimensions, proceeds at a same rate for both groups. EC and IC animals apparently do not differ with respect to the learning of simple spatial discrimination per se. This indicates that an increase in the α-value, or an increase in the associability of the relevant stimulus through reinforcement proceeds at the same rate for both EC and IC animals, and that with a minimum of irrelevant stimulation that receives 0% reinforcement, IC animals are still capable to reduce the α-value of this irrelevant stimulation sufficiently.

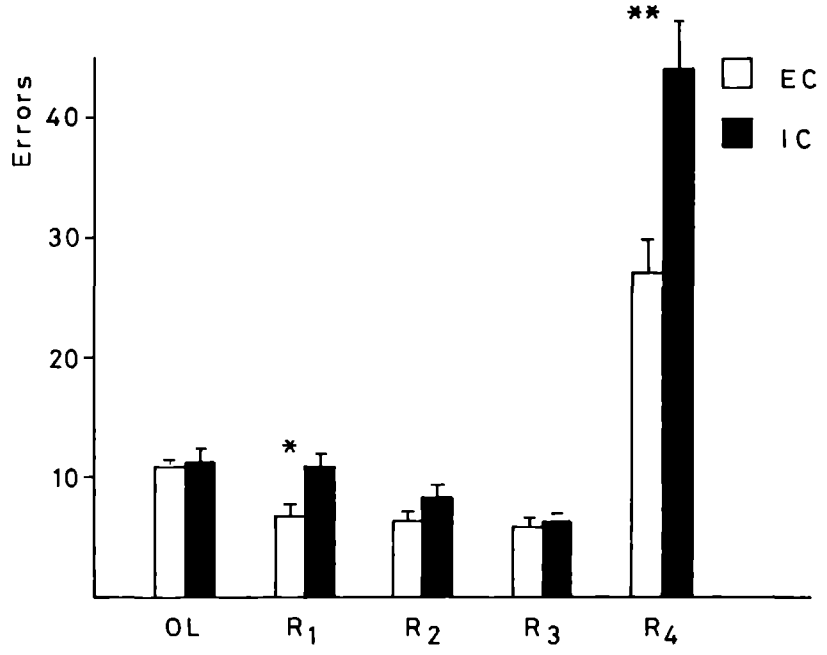

Figure 5.7. Mean number of errors (± SEM) for EC and IC rats on the acquisition of a spatial discrimination problem (OL), on subsequent spatial reversal problems (R1, R2 and R3: intradimensional shifts) and on a subsequent visual discrimination problem (R4: extradimensional shift). $^{*}p < 05$ $^{**}p < 01$

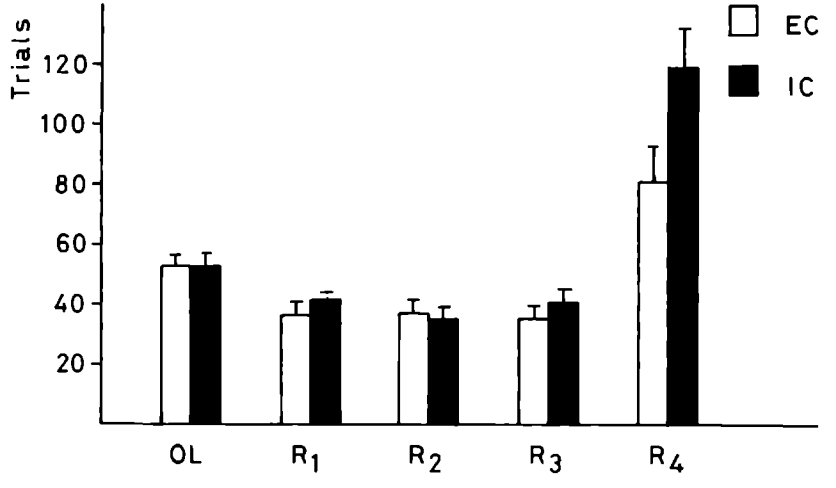

Figure 5.8. Mean number of trials (± SEM) for EC and IC rats on the acquisition of a spatial discrimination problem (OL), on subsequent spatial reversal problems (R1, R2 and R3: intradimensional shifts) and on a subsequent visual discrimination problem (R4: extradimensional shift).

Again, as in experiment 1, EC animals make fewer errors than IC animal do at the first reversal problem (R1). As for the number of trials needed no differences are found. Thus, it may be concluded that, as in experiment 1, during reversal learning EC animals cannot switch as fast from relevant to irrelevant and vice versa within the same stimulus dimension, since IC animals keep responding longer to the initially relevant stimulus. Apparently, IC animals are less capable of reducing the α-value of a stimulus in response to its contingency with nonreinforcement. However, with each additional reversal, the reversal learning performance of IC animals becomes more similar to that of EC animals. It appears that within a certain stimulus dimension the reduction of the α-value of stimuli that have become irrelevant requires a learning process that in IC animals proceeds slower than in EC animals. Following the first reversal this reduction develops in IC animals as fast as in EC animals, a phenomenon observed in experiment 1 also. If, however, the stimulus dimension is changed too (R4, EDS), EC animals show better learning performance than IC animals again. This difference is significant as to number of errors made and approaches significance with respect to number of trials needed. During the extradimensional shift the subjects are exposed to several irrelevant stimuli, the α-values of which have to be reduced. Moreover, both place stimuli, left and right, are 50% reinforced.

The occurrence of differences between EC and IC subjects in learning performance appears to depend upon the presence or absence of multiple stimulus dimensions that may be involved in the development of strategies for the solution of the discriminative problem. Further, the learning differences in reversal learning seem to be caused by a slower switching of the cues from relevance to irrelevance in IC animals.
So, if EC and IC animals have to learn a spatial discrimination in the presence of several irrelevant (visual) stimuli a difference between EC and IC animals will have to become apparent already during the initial learning of the spatial discrimination. This will be examined in experiment 3.

5.4. EXPERIMENT 3. EFFECTS OF DIFFERENTIAL EXPERIENCE IN ENRICHED (EC) AND IMPOVERISHED (IC) ENVIRONMENTS ON SPATIAL DISCRIMINATION AND REVERSAL LEARNING IN THE PRESENCE OF IRRELEVANT BRIGHTNESS DISCRIMINATIVE STIMULI

5.4.1. INTRODUCTION

The results of the experiments 1 and 2 demonstrate that TMB rats solve a spatial discrimination problem in the KMDB faster than a visual discrimination problem. On the one hand, this might be explained by assuming that TMB rats have higher α-values for spatial stimuli than for brightness

stimuli. On the other hand, the amount of irrelevant stimulation may have played a part too.
In this experiment, the animals are exposed to similar spatial discrimination tasks as in experiment 2; however, now irrelevant brightness discriminative stimuli are present also. We expect that IC rats will solve the spatial discrimination slower because of the presence of these irrelevant stimuli. This expectation is based on our hypothesis (chapter 1, 1.8) that IC animals possess a stimulus selection system that functions less efficiently, particularly with respect to the inhibition of irrelevant stimuli.

5.4.2. METHODS

Subjects
24 male TMB rats were used: 12 EC reared animals and their 12 IC reared littermates. The animals remained in their respective environments during 37 days, from weaning (at an age of approximately 24 days) onwards. The environments used, group assignment procedures and rearing conditions are described in chapter 2.
After termination of the differential rearing all animals were rehoused individually in IC-type macrolon cages. Three days later behavioural tests started.

Apparatus
The pre-training runway and the KMDB were identical with those used in experiments 1 and 2 (5.2.2, figure 5.1 and 5.2).

Procedure
Pre-training and discrimination and reversal training procedures were identical with those employed in experiment 2. Whereas in experiment 2 all alleys were illuminated, in this experiment at each choice point the animal was confronted with one light and one dark alley. The light-dark pattern of the alleys, which differed on each trial, was similar to the one used in experiment 1. This brightness difference constituted an irrelevant stimulus during OL, R1, R2 and R3; in these tasks the animal had to learn a spatial discrimination. On day 5, during R4, however, an extradimensional shift was introduced: now the animals had to learn a brightness discrimination. The illuminated alley was the correct choice.

5.4.3. RESULTS

Pre-training
Mean latency per trial from day 4 to 9 is given in figure 5.9. From this graph it can be deduced that EC animals go through the alley faster than IC animals do. An analysis of variance revealed that each day the differences between EC and IC animals were significant (day 4: $F(1,11)=25.89$; $p<.001$; day 9: $F(1,11)=9.16$; $p<.05$).

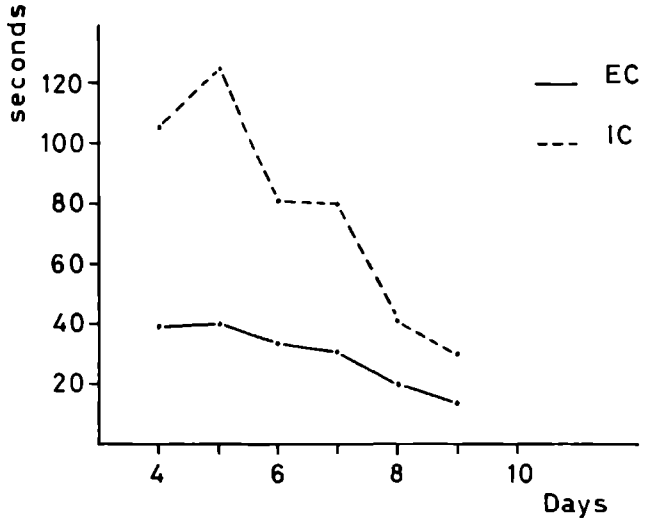

Figure 5.9. Mean latency (in seconds) a day for EC and IC rats during pre-training.

Discrimination and reversal learning

Figure 5.10 depicts the mean number of errors made by EC and IC animals during OL, R1, R2, R3 and R4. Analyses of variance revealed that in the presence of irrelevant light-dark stimuli, EC animals make significantly less errors than IC animals do while learning a spatial discrimination ($F(1,11)=7.47$; $p<.05$). This difference remains at a significant level during the first and second reversals (intradimensional shifts; R1: $F(1,11)=6.48$; $p<.05$; R2: $F(1,11)=5.05$; $p<.05$). During the third reversal (R3) the difference in the number of errors has become smaller and no longer reaches significance. During R4, the extradimensional shift, no differences between EC an IC animals were found. As to the number of trials needed (figure 5.11) EC and IC animals never differed; only during OL was significance approached ($F(1,11)=3.39$; $p<.1$).

Comparing the OL results of the EC and IC animals in the present experiment with those obtained in experiment 2 (Mann-Whitney U-test), both EC groups do not differ and neither do both IC groups. However, in this comparison groups do not represent a split-litter design.

Comparing the R4 results of EC animals of experiment 2 with those of the present experiment, it becomes clear that the EC animals of the present experiment make more errors than those of experiment 2, at an almost significant level ($p<.1$, Mann-Whitney U-test).

5.4.4. DISCUSSION

When TMB rats are exposed to a spatial discrimination problem in the presence of irrelevant visual stimuli, they

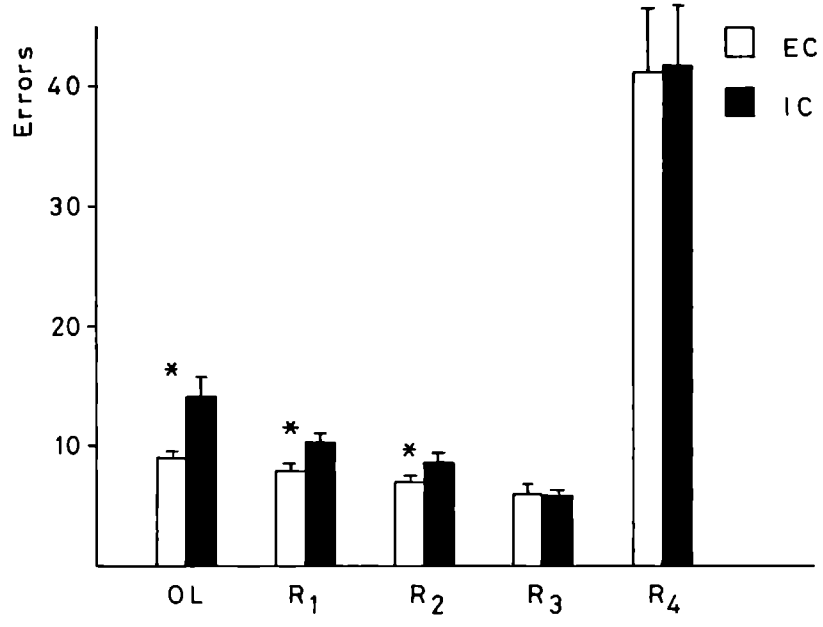

Figure 5.10. Mean number of errors (± SEM) for EC and IC rats on the acquisition of a spatial discrimination problem (OL), on subsequent spatial reversal problems (R1, R2 and R3: intradimensional shifts) and on a subsequent visual discrimination problem (R4: extradimensional shift). During the spatial discrimination and reversal problems irrelevant visual stimuli were present. *p< 05

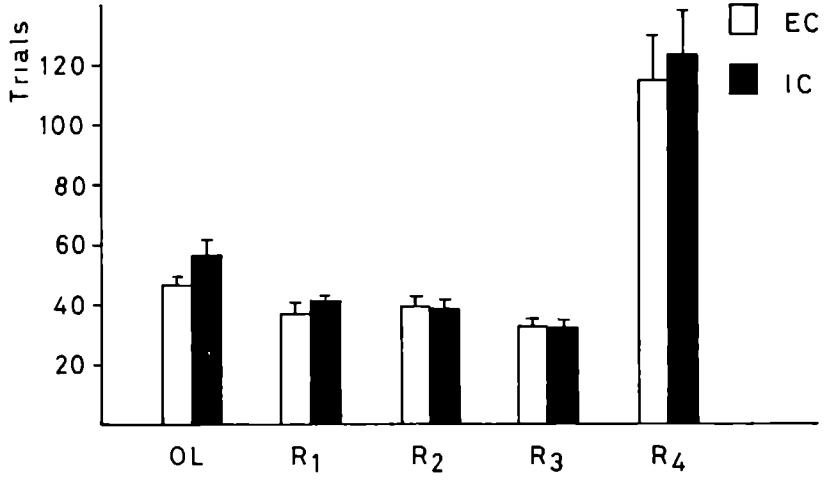

Figure 5.11. Mean number of trials (± SEM) for EC and IC rats on the acquisition of a spatial discrimination problem (OL), on subsequent spatial reversal problems (R1, R2 and R3): intradimensional shifts) and on a subsequent visual discrimination problem (R4: extradimensional shift). During the spatial discrimination and reversal problems irrelevant visual stimuli were present.

learn the spatial discrimination almost as well as they did in experiment 2, in the absence of irrelevant stimuli, and much better than they did in experiment 1. This is a strong indication that in TMB rats the α-values for spatial stimuli are indeed higher (probably genetically determined) than those for brightness stimuli. In contrast with experiment 1, differences between EC and IC animals during initial learning were found this time. This can be explained only through the presence of irrelevant visual stimulation, since in experiment 1 no differences in the learning performances of both groups in the absence of irrelevant stimulation were found. The amount of irrelevant stimulation appears to negatively influence the selection of the relevant discriminative stimulus. Again this indicates that IC animals are less capable to lower the α-values for irrelevant brightness cues, light and dark, if those stimuli are correlated with nonreinforcement (in 50% of the trials). The difference between EC and IC animals as to number of errors made during the first reversal, and the disappearance of this difference during subsequent reversals, replicates the results of experiment 2. In contrast with experiment 2, however, EC and IC animals still differ during the second reversal as to the number of errors made, though during the third reversal the difference is gone. These findings again, indicate that the inhibition of irrelevant stimuli succeeds less well initially in the IC animals, although later on, after additional reversals, they no longer differ from EC subjects.

A remarkable result from this experiment is that during R4, the extradimensional shift, EC and IC rats do not differ at all. Comparison of these results with those obtained in the experiments 2 and 3, gives rise to the suspicion that the absence of any difference between EC and IC animals during the EDS is caused by the poorer performance of the EC animals from the present experiment as compared with those from experiment 2. In the R4 of experiment 2 the animals were for the first time confronted with two discriminative stimulus dimensions (location and brightness). Both stimulus dimensions have been present all the time during the various tasks in experiment 3. An explanation for the present absence of differences between EC and IC animals during the extradimensional shift, might be that EC animals are handicapped by their better functioning stimulus selection mechanism, through inhibition of the irrelevant stimuli. From OL to R3 the EC animals have learned more clearly than IC animals that brightness is an irrelevant cue. Thus, they have more difficulty to base their learning during R4 on the brightness cue: the α-value of the light stimulus has to rise from a lower level in EC animals than in IC animals. However, in the present experiment as well as in experiment 2, EC animals are more capable than IC animals of suppressing the α-value of the spatial stimulus that was relevant before and still is 50% reinforced. Both phenomena contribute to the final learning performance of EC and IC animals in the EC being equal. If we compare the performances of the IC animals from experiments 2 and 3, no differences are found.

In conclusion: from the experiments 1, 2 and 3 the following suggestions can be deduced:

- TMB rats probably possess a -genetically determined- higher α-value for spatial stimuli than for brightness stimuli. This strain's preference for spatial hypotheses over brightness hypotheses (Krech et al., 1954) may be explained this way. Also, it is conceivable that during the original selection and breeding for maze learning performance (in a multiple T-maze) Tryon (1940) unknowingly selected for the possession of higher α-values for spatial stimuli.
- IC rats are less able than EC rats to efficiently lower the α-value of irrelevant stimuli, when these stimuli are contingent with nonreinforcement.
- EC and IC animals do not differ with respect to the efficient enhancement of the α-value of the relevant stimulus when this stimulus is contingent with reinforcement.

CHAPTER 6

EFFECTS OF DIFFERENTIAL EXPERIENCE IN ENRICHED (EC) AND IMPOVERISHED (IC) ENVIRONMENTS ON LATENT INHIBITION AND THE LEARNING OF A TWO-WAY ACTIVE AVOIDANCE RESPONSE IN THE SHUTTLE BOX

6.1. INTRODUCTION

In the context of our research into the effects of differential experience with EC and IC environments on inhibition of irrelevant stimuli, resulting in the omission of behaviour, and particularly on the role of stimulus selection therein, we decided to examine the effects of CS pre-exposure upon learning behaviour of EC and IC animals. Pre-exposure to a CS prior to the use of that CS in a learning task, results in a retarded acquisition of the response to be learned (Lubow and Moore, 1959; Lubow, 1973). This phenomenon is called inhibitory preconditioning or latent inhibition. Thus, latent inhibition as a term describes the process that is thought to underly the retarded conditioning as a consequence of nonreinforced exposure to the stimulus prior to conditioning. The simple presentation of a stimulus that later on is going to serve as a CS, i.e. prior to it being paired with an unconditioned stimulus (US), retards the development of a conditioned response (CR) when the CS and US finally are paired. Latent inhibition has, among others, been observed during the acquisition of an avoidance response in a two-way active avoidance problem in a shuttle box. Subjects which in the situation described had been pre-exposed several times to a tone (CS) before the start of the actual conditioning procedure acquired the conditional avoidance response (CAR) at a slower rate than did controls that had never been pre-exposed to the tone (Ackil et al., 1969; Feldman, 1977). The phenomenon of latent inhibition has been explained along two main lines: an associative intepretation and a nonassociative interpretation (Halgren, 1974). Initially, the associative interpretation suggests that nonreinforced presentations might turn the stimulus automatically into a conditioned stimulus for some, mostly unknown, behaviour that develops during the pre-exposure (this behaviour thus becomes a conditioned response, comparable with "superstitious" behaviour). During the proper conditioning process, this behaviour first has to be extinguished before any new response can be learnt (Lubow and Moore, 1959; Lubow, 1965).
More recent experiments departing from the theory of context specifity of conditioning and extinction, gave rise to the suggestion that latent inhibition still represents an associative process, the associations established being between contextual stimuli and the pre-exposed stimulus (Wagner, 1979). Wagner assumes that these associations retard the formation of an association between the pre-exposed CS and the unconditioned stimulus (US). The

theorizing on context specificity assumes that during learning and conditioning, the development of CS-US associations, the context plays an important role. It is assumed that conditioning does not take place in isolation, but against the background of other stimuli, the context (Asratyan, 1965; Bouton and Bolles, 1979; Balaz et al., 1981). This context contains stimuli, for example, of the experimental setting (colour and material of the walls of the testcage, illumination, odours), the experimenter, as well as interoceptive stimuli, concerning the motivational state of the subject, time during the diurnal cycle etc. The theory assumes that these contextual stimuli serve as cues for the retrieval process, to retrieve CS-US relationships and bring them into awareness. Thus, there is evidence that rats that have to relearn an acquired conditioned response in the same environment in which the original acquisition had taken place, do this easier and with less errors than animals which have to relearn the same conditioned response in a situation that differs from the original learning situation. Wagner suggests that during the pre-exposure of the CS associations are formed between that CS and contextual stimuli, which associations disrupt the subsequent formation of associative connections with the US. Thus, when pre-exposure and conditioning of the CS occur in the same environment/context, much more latent inhibition is found than when pre-expoosure and conditioning are carried out in different contexts (Channel and Hall, 1983; Hall and Minor, 1984).

The nonassociative interpretation elaborates the idea that prior presentations of the CS render this stimulus less salient, or less able to gain attention, less signalling. This might interfere with the formation of associations between the stimulus with other stimuli or with behaviours (Rescorla, 1971); or, the animal might habituate to the stimulus and thus fail to pay attention to the stimulus (Lubow, 1965). This interpretation regards latent inhibition as a form of attentional decrement.

In this context, Mackintosh's (1973) learned-irrelevance hypothesis is of interest (see chapter 5, 5.1). This hypothesis fits in the class of nonassociative interpretations. Mackintosh assumes that the subject learns to ignore the pre-exposed stimulus, which renders this stimulus less able to enter into new associations with for example responses, without that stimulus developing inhibitory properties. In terms of Mackintosh's theory (1975), the α-value of the pre-exposed stimulus declines further and further during the pre-exposure, since during pre-exposure each presentation is contigent with nonreinforcement. When acquisition of the learning problem starts, animals that have had CS pre-exposure, start with much lower α-values for the CS than do non pre-exposed controls, which interferes with the rate of acquisition.

Recent studies which aimed to determine which of both interpretations mentioned is correct, initially pointed towards the non-associative interpretations (Wagner and Rescorla, 1972, pages 326-330; Halgren, 1974; Solomon et al., 1974; Feldman, 1977). Therefore, latent inhibition is a

behavioural phenomenon of considerable interest for our research into possible differences between EC and IC rats as to their efficiency of stimulus selection, particularly with respect to the inhibition of irrelevant stimuli (caused by a decrement of the α-value of those stimuli not correlated with reinforcement). In the research described before (chapter 5) indications that point in that direction have been found.

It has been shown that the administration of scopolamine results in the abolishment of the effects of CS pre-exposure (Carlton, 1969; see also Lubow, 1973). Following pre-exposure to the CS, animals thus treated acquire a two-way active avoidance response quicker than nontreated subjects. Animals with hippocampal lesions learn a two-way active avoidance problem after CS pre-exposure as fast as without any pre-exposure (Ackil et al., 1969). In view of the assumption of Douglas (1972) and Warburton (1972) that animals with hippocampal lesions and animals treated with scopolamine both possess badly functioning cholinergic systems, the data published by Carlton and Ackil et al. support our expectation that after pre-exposure to the CS IC animals will show better learning performance than EC animals during the acquisition of a two-way active avoidance response.

Before examining the effects of pre-exposure to the CS upon the learning performance of EC an IC animals in the shuttle box, it was first investigated whether EC and IC animals would differ in the learning of a two-way active avoidance response without any pre-exposure at all.

Evidence concerning two-way active avoidance behaviour in EC and IC animals or in IC and group-reared animals is scarce and contradictory. Lovely et al. (1972) compared animals reared in isolation (IC) with animals reared in a standard laboratory condition (SC). In animals reared in isolation they observed a faster acquisition and slower extinction of the two-way active avoidance behaviour (with a tone CS). Freeman and Ray (1972) found a heredity effect in the acquisition of a two-way active avoidance response in a shuttle box (using a light CS). F 344 rats acquired the response quicker than Zivic-Miller rats. Animals of both strains had been reared in EC or standard laboratory conditions (SC) for 60 days from weaning onwards. In the Zivic-Miller strain the EC rats performed better than the SC controls, whereas in the F 344 strain the SC group did better than the EC group. Doty (1972) compared the learning performance of approximately two year old EC and SC rats. She did not observe a difference between EC and SC rats in the acquisition of a two-way active avoidance response (using a light CS). Ray and Hochhauser (1969) also examined the two-way active avoidance behaviour of EC and SC rats. Their subjects received 25 trials a day on six consecutive days; a light served as the CS. They reported that EC rats showed better learning performance, but the difference appeared only on the 5th and 6th days. However, before training in the shuttle box started, these animals had been extensively studied in other learning tasks. Ferchmin et al. (1980) did not find any effects of differential experience

with EC and IC environments on two-way active avoidance conditioning in the shuttle box.
Form these contradictory reports no clear picture is to be derived whether - and if so to what degree - EC and IC rats differ as to the acquisition of a two-way active avoidance response in a shuttle box.

6.2. EXPERIMENT 1. EFFECTS OF DIFFERENTIAL EXPERIENCE IN ENRICHED (EC) AND IMPOVERISHED (IC) ENVIRONMENTS ON THE LEARNING, RELEARNING AND EXTINCTION OF A TWO-WAY ACTIVE AVOIDANCE RESPONSE, WITH AND WITHOUT CS PRE-EXPOSURE

In this experiment the acquisition of a two-way active avoidance response will be examined in EC and IC animals. The relearning of this response after a 24-hours interval and the extinction of this response will be studied also.

6.2.1. METHODS

Subjects
Fourteen littermate diplets of male TMB rats were used. Fourteen animals had been reared in an EC condition, the other fourteen in an IC condition. The animals had lived in their respective environments for 39 days, from an age of ± 28 days onwards. Procedures employed in group assignment (split-litter design) and rearing in the respective environments have been described in chapter 2. 10 subjects (five littermate diplets, five of which came from the EC condition and their five littermates from the IC condition) were not pre-exposed to the CS. The other 18 subjects (9 littermate diplets) received pre-exposure to the CS.

Apparatus
The animals were trained and tested in a shuttle box of 40*25*45 cms, made of plexiglass. The floor of the shuttle box consisted of a grid of 20 steel rods, placed at distances of 1 cm each. The cover was made of plexiglass and contained a number of air holes. The shuttle box was divided into two identical compartments of 20*25*45 cms each by a barrier of 3 cms high on the floor.
A shock-scrambler provided a shock (the UCS) of 0.4 mA. As the CS served a tone of 4000 Hz and 75 dB, which lasted 5 seconds. The tone was presented through a speaker with a diameter of 6 cms. This speaker was mounted high against one of the sidewalls over the barrier. Back ground noise was approximately 45 dB. The box was illuminated with a red 100 W bulb, mounted ± 40 cms above the top of the box. Behavioural observations were made from behind a one-way screen.

Procedure
All subjects were tested on two consecutive days.
Animals that were not pre-exposed to the CS were trained as follows: on the first day of training each animal was placed

in the shuttle box and during 15 minutes the animal could explore the box. Following these 15 minutes of habituation time the acquisition phase (L1) started. The 5 second CS was presented automatically at a fixed intertrial interval of 30 seconds. If after the 5 seconds CS the animal was still at the same side of the shuttle box, a shock (of maximally 20 seconds) was delivered through the grid. The animal could escape from the shock by going to the other compartment of the box which at that time was not electrically charged (escape response). If an animal departed to the other compartment within 5 seconds after the onset of the CS, it could avoid the shock (avoidance response). The learning criterion was reached as soon as the animals made eight avoidance responses in a series of 10 successive trials. If the subject had reached criterion, an additional of 15 trials were given after which it was removed from the shuttle box. 24 hours later (on the second day of testing) the animal was again placed in the shuttle box and after two minutes the relearning procedure (L2) started. The animal had to relearn the response learned on the first day of testing, the training procedure being identical. As soon as the 8/10 criterion was reached, extinction training (Ext) started. The extinction procedure differed from the training procedure only in that during extinction a CS was never followed by shock. The extinction criterion was reached when in 10 successive trials the animals made no more than two avoidance responses.
The animals that were given CS pre-exposure were treated slightly differently. During the 15 minutes of habituation in the shuttle box on the first day of training, before the start of the learning procedure (L1), these subjects were given 25 presentations of 5 seconds each of the tone CS, with a fixed intertrial interval of 30 seconds. After this pre-exposure during 15 minutes, learning (L1) started, followed by the relearning procedure (L2) and the extinction procedure (Ext) on the next day as described above.

6.2.2. RESULTS

First, we will compare the EC and IC animals which did not receive pre-exposure to CS. Mean number of errors and mean number of trials needed till criterion for the phases L1, L2 and Ext are depicted in figure 6.1. Figure 6.2. shows the mean number of avoidance responses per 10 trials during the three phases for EC as well as IC animals. Group differences were tested by means of analyses of variance. EC and IC animals did not differ as to number of errors made and number of trials needed, neither during L1 nor during L2 and Ext of a two-way active avoidance response.
Secondly, the results of EC and IC animals which received a pre-exposure treatment will be considered. Mean number of errors and mean number of trials needed to reach criterion during L1, L2 and Ext are shown in figure 6.3. Figure 6.4. represents the mean number of avoidance responses per 10 trials during the L1, L2 and Ext phase for EC and IC

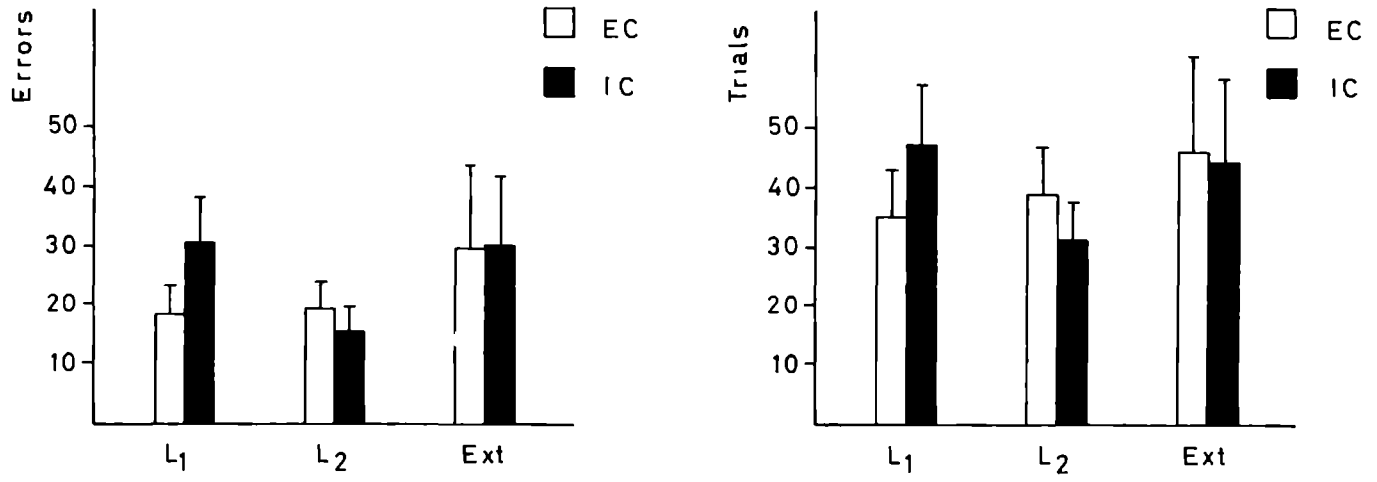

Figure 6.1. Mean number of errors (± SEM) and mean number of trials (± SEM) for EC and IC rats on the acquisition of a two-way active avoidance problem (L1), and on relearning (L2) and extinction (Ext) of the problem, without pre-exposure of the CS.

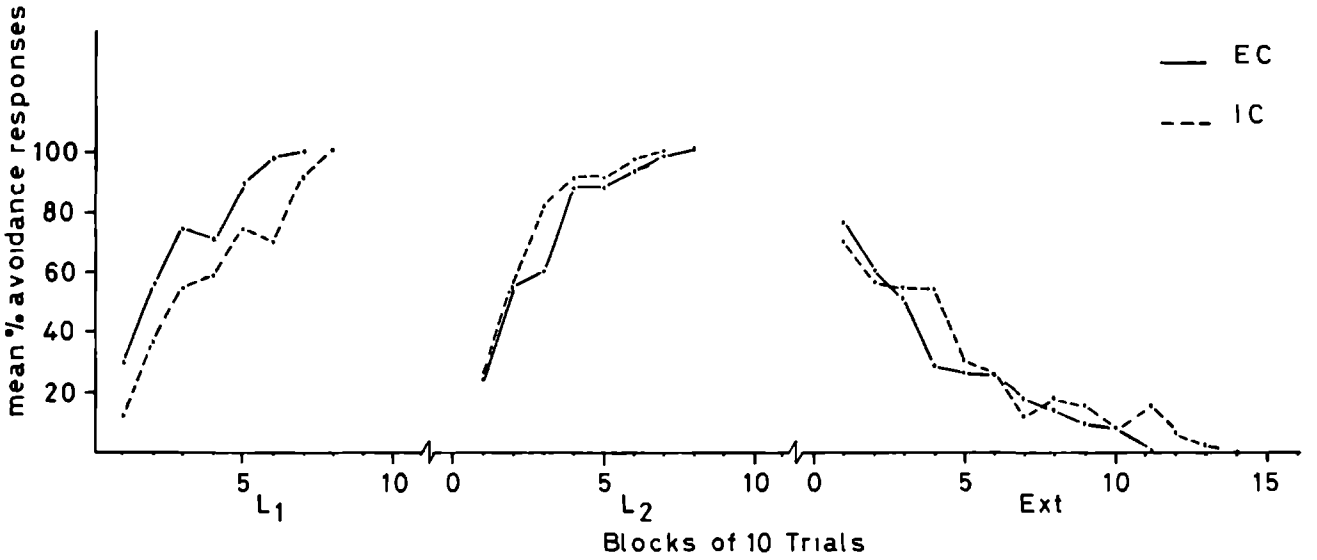

Figure 6.2. Mean percentage of avoidance responses over blocks of 10 trials for EC and IC rats on the acquisition of a two-way active avoidance problem (L1), and on relearning (L2) and extinction (Ext) of the problem, without pre-exposure of the CS.

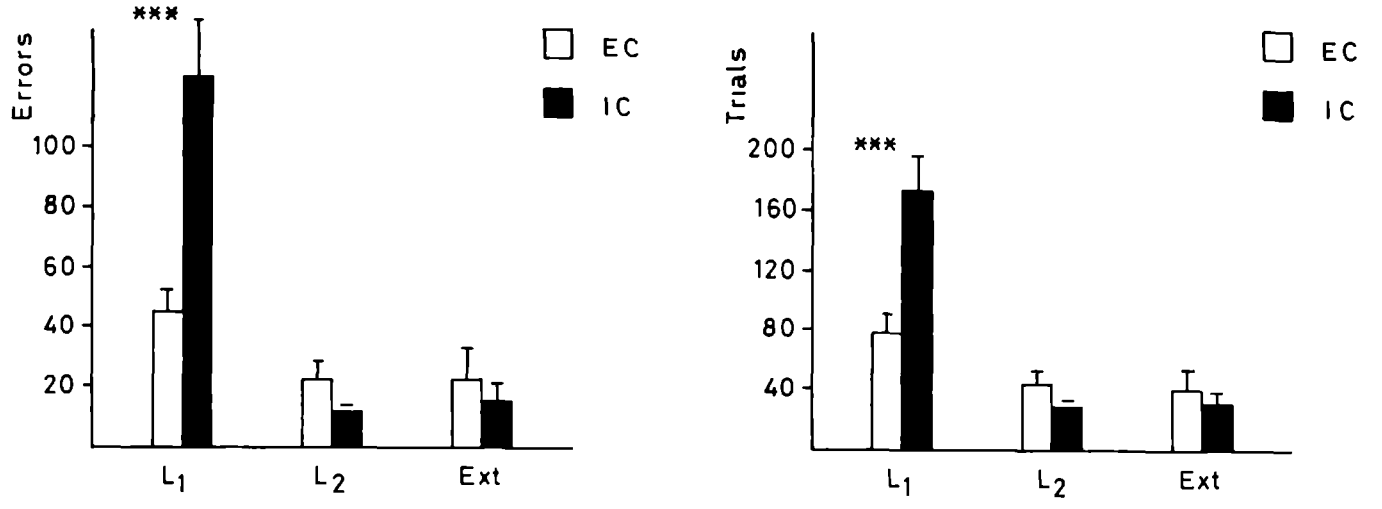

Figure 6.3. Mean number of errors (± SEM) and mean number of trials (± SEM) for EC and IC rats on the acquisition of a two-way active avoidance problem (L1), and on relearning (L2) and extinction (Ext) of the problem, with pre-exposure of the CS.
***p< 001

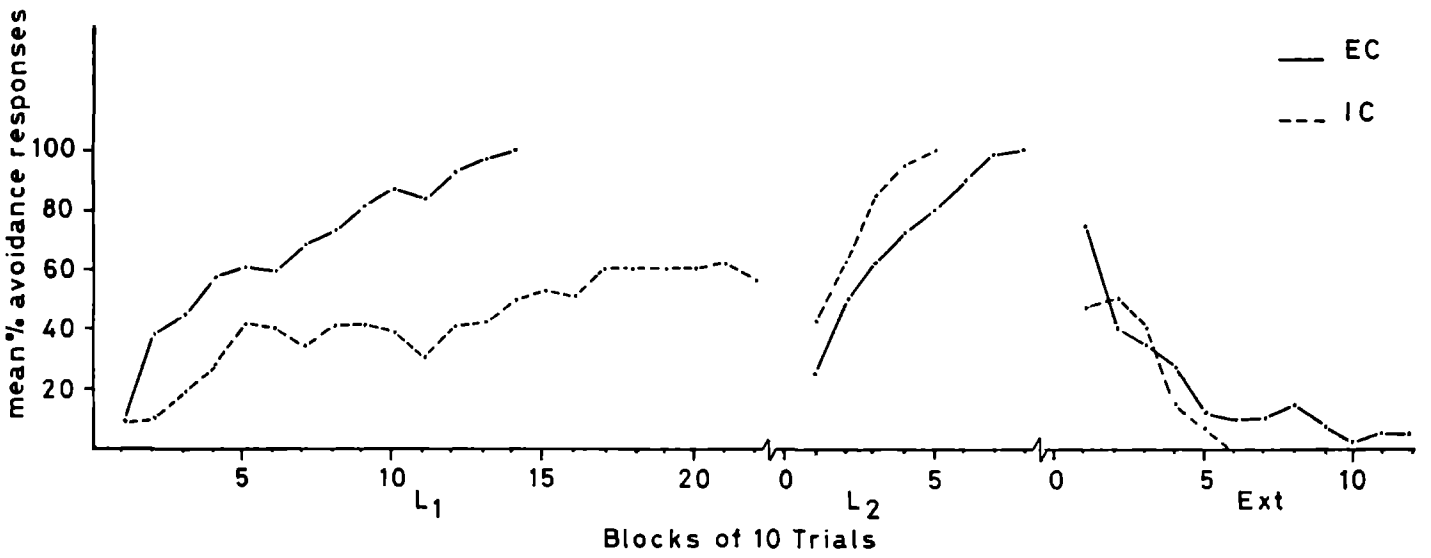

Figure 6.4. Mean percentage of avoidance responses over blocks of 10 trials for EC and IC rats on the acquisition of a two-way active avoidance problem (L1), and on relearning (L2) and extinction (Ext) of the problem, with pre-exposure of the CS.

animals. Group differences were tested by means of analyses of variance.
During the learning (L1) of the avoidance response in a two-way active avoidance situation after CS pre-exposure EC and IC animals differ greatly. IC rats make significantly more errors ($F(1,8)=22.903$; $p<.001$) and need significantly more trials ($F(1,8)=27.801$; $p<.001$) to reach criterion than do EC animals.
Five IC animals did not reach criterion at all and hence could not be retested for relearning and extinction performances. All other differences between EC and IC animals, number of errors made and number of trials needed, did not reach significance.
If we compare both EC groups and both IC groups with each other, it becomes clear that pre-exposure to the CS resulted in impaired learning performance in EC animals as well as in IC animals; this is revealed in number of errors as well as in number of trials needed; EC: errors, $U=6.5$, $p<.05$; trials, $U=6$, $p<.05$; IC: errors, $U=2$, $p<.02$; trials, $U=2$, $p<.02$ (Mann-Whitney U-test).
In view of those intriguing and unexpected results, it was decided to repeat the experiment. More animals were employed and an easier learning procedure was used. The CS was presented at a variable interval and lasted for maximally 25 seconds during L1 and L2 and a maximum of 5 seconds during the extinction phase. CS presentation lasted maximally 25 seconds or until the animal made an avoidance or escape response. At that moment the tone (and in the case of an excape response also the shock) was terminated. It appears that generally avoidance conditioning proceeds more rapidly under this regime than under the regime employed in experiment 1, in which the execution of an avoidance response did not immediately terminate the tone CS (Bower et al., 1965). Thus, we expect that in this replication experiment better results will be obtained and fewer animals will fail to reach criterion.

6.3. EXPERIMENT 2. EFFECTS OF DIFFERENTIAL EXPERIENCE IN ENRICHED (EC) AND IMPOVERISHED (IC) ENVIRONMENTS ON THE LEARNING, RELEARNING AND EXTINCTION OF AN ACTIVE AVOIDANCE RESPONSE WITH AND WITHOUT PRE-EXPOSURE TO THE CS: A MODIFICATION AND REPLICATION

6.3.1. METHODS

Subjects
In this experiment 40 male rats of the TMB strain were used: 20 animals had been reared in an EC condition, their 20 littermates came from IC environments. The animals had stayed in the respective environments for approximately 30 days, from an age of ± 30 days onwards. Procedure of group assignment of this split-litter design as well as rearing method in the various environments are described in chapter 2.

20 subjects (10 littermate diplets, 10 of which came from the IC condition, their 10 littermates coming from the EC condition) were trained without prior exposure to the CS, the other 20 animals were trained in a two-way active avoidance situation after pre-exposure to the CS.

Apparatus
The shuttle box, shock (US) and tone signal (CS) used here are identical with those employed in experiment 1.

Procedure
Learning and extinction procedures were almost identical with those used in experiment 1. The main differences are that now the CS is presented during maximally 25 seconds and at a variable intertrial that varies from 30-60 seconds (mean 45 seconds) during the learning and relearning phase, whereas during extinction the CS does not last longer than 5 seconds. Moreover, the CS was terminated at the very moment an animal made an escape or avoidance response.

6.3.2. RESULTS

First, the results of EC and IC animals that did not receive pre-exposure to CS will be considered. The mean number of errors made, mean number of trials needed and the mean number of intertrial crossings per trial made during the respective L1, L2 and Ext phases are presented in Figure 6.5. Figure 6.6 also depicts the mean number of avoidance responses per 10 trials during L1, L2 and Ext for both the EC and the IC animals. Differences between groups were tested by means of analyses of variance. During the initial acquisition of the two-way active avoidance response the learning performance of EC and IC animals do not differ, just as they did not in experiment 1. However, the tendencies are in the same directions as those found in experiment 1. During the relearning of the response 24 hours later (L2), IC rats perform better than EC rats do. These differences are significant: the IC animals make fewer errors ($F(1,9)=9.244$, $p<.05$) and reach criterion more rapidly ($F(1,9)=8.669$, $p<.02$) than EC animals do. During the extinction phase EC and IC animals do not differ.
Now, we will consider the results of the EC and IC animals that have had prior exposure to the CS. Mean number of errors made, and mean number of trials needed during L1, L2 and Ext are presented in figure 6.7. Figure 6.8 also depicts the mean number of avoidance responses per 10 trials during learning, relearning and extinction, for EC as well as IC animals. Again, group differences were tested by means of analyses of variance.
Just as in experiment 1, a clear difference between EC and IC rats was observed during acquisition of an avoidance response in a two-way active avoidance situation after prior exposure to the CS. IC rats make significantly more errors ($F(1,9)=24.751$, $p<.001$) and need significantly more trials to reach criterion ($F(1,9)=27.239$, $p<.001$) during L1 than EC

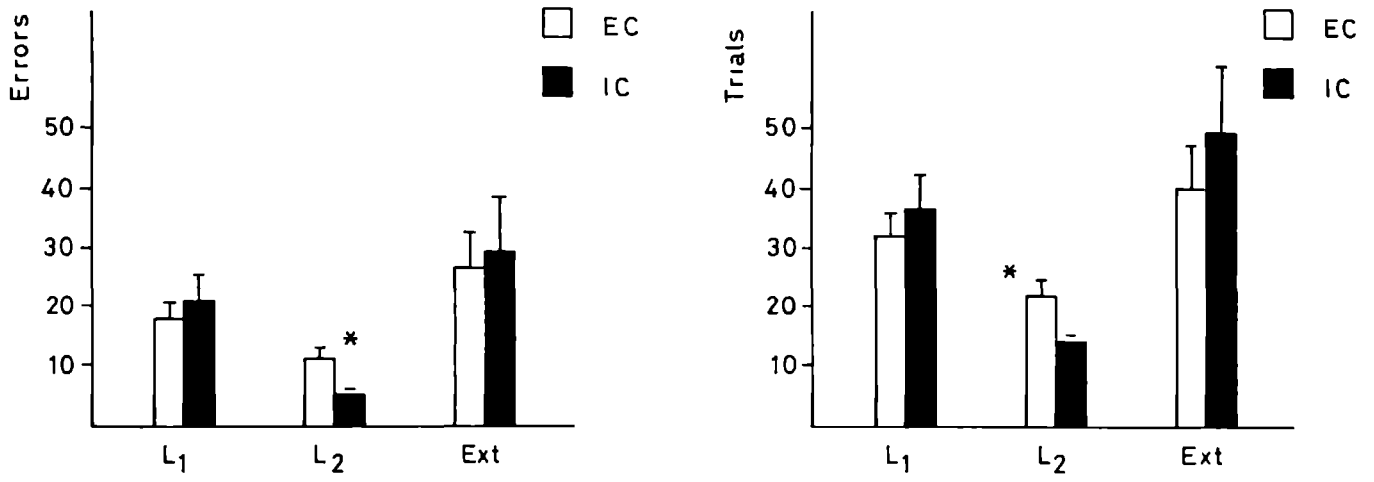

Figure 6.5. Mean number of errors (± SEM) and mean number of trials (± SEM) for EC and IC rats on the acquisition of a two-way active avoidance problem (L1), and on relearning (L2) and extinction (Ext) of the problem, without pre-exposure of the CS.
*$p < 05$

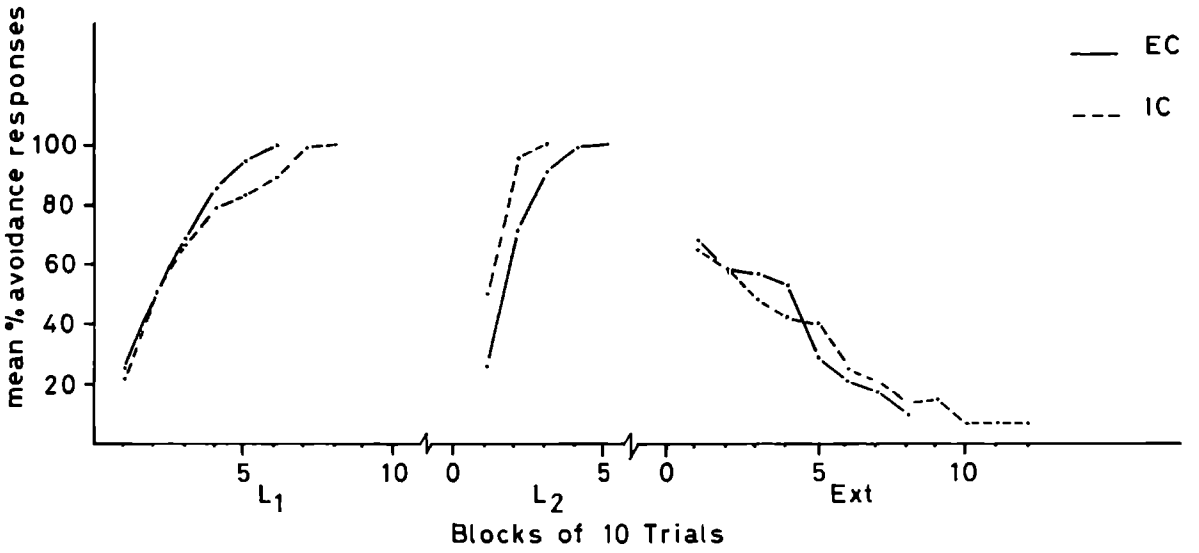

Figure 6.6. Mean percentage of avoidance responses over blocks of 10 trials for EC and IC rats on the acquisition of a two-way active avoidance problem (L1), and on relearning (L2) and extinction (Ext) of the problem, without pre-exposure of the CS.

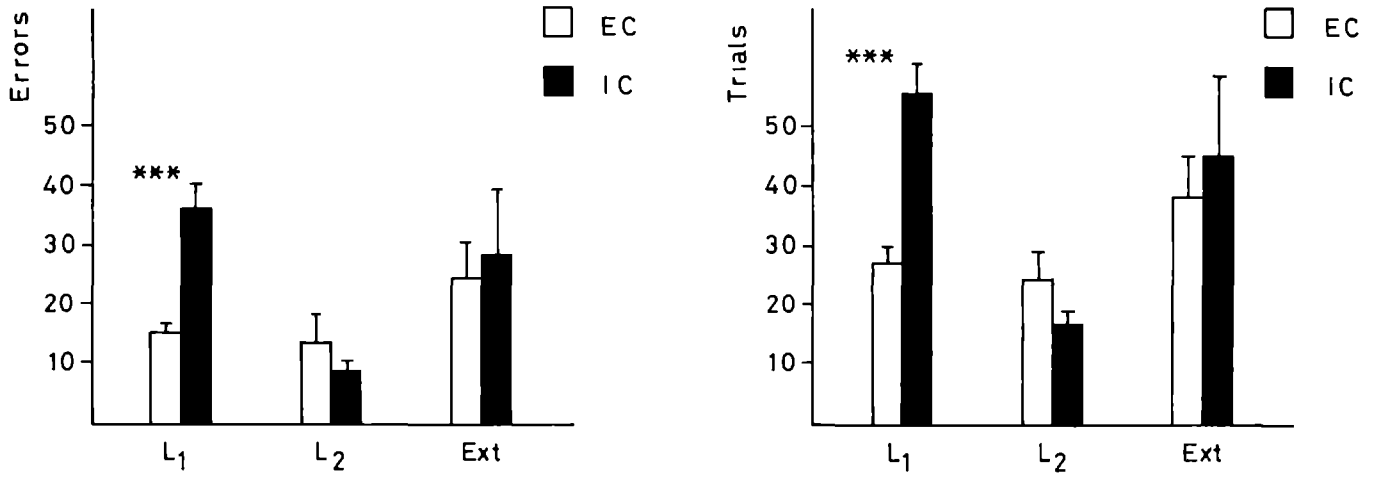

Figure 6.7. Mean number of errors (± SEM) and mean number of trials (± SEM) for EC and IC rats on the acquisition of a two-way active avoidance problem (L1), and on relearning (L2) and extinction (Ext) of the problem, with pre-exposure of the CS.
***$p < 001$

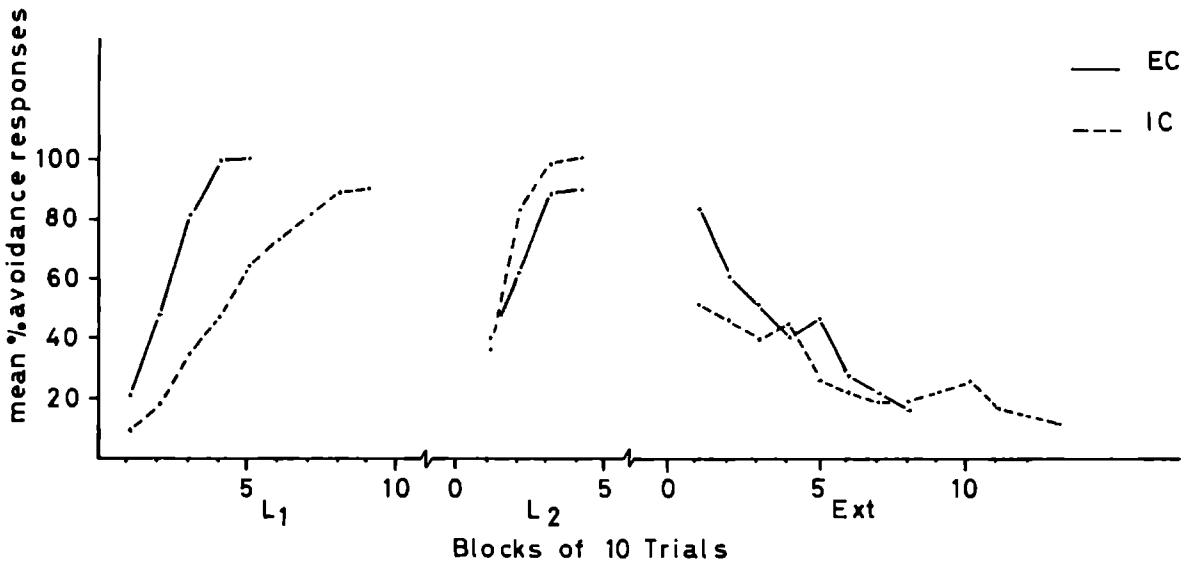

Figure 6.8. Mean percentage of avoidance responses over blocks of 10 trials for EC and IC rats on the acquisition of a two-way active avoidance problem (L1), and on relearning (L2) and extinction (Ext) of the problem, with pre-exposure of the CS.

rats do. All other diferences between EC and IC subjects during L2 and Ext do not reach significance.
When we compare both EC groups and both IC groups, it is clear that this time pre-exposure to the CS does not affect the performance of the EC group, whereas it leads to an impaired performance of the IC group, as far as number of errors ($U=16.5$, $p<.02$) as well as trials needed ($U=15.5$, $p<.02$) is concerned. During relearning and extinction no differences between the two EC groups and IC groups were observed.

6.4. DISCUSSION

In general, it can be concluded that EC and IC animals do not differ in the acquisition of a two-way active avoidance response in a shuttle box. It is evident that EC and IC animals differ, however, with respect to the effect of pre-exposure to the CS on conditioning. Contrary to our expectations, IC animals appear to exhibit poorer learning performance after a prior CS-exposure, whereas during a more optimal training procedure EC rats do not give the slightest sign of latent inhibition at all. These findings might entirely undermine our hypothesis concerning a less efficient suppression of irrelevant stimuli in IC animals, were it not that very recent studies from the Mackintosh group (Lovibond et al., 1984) indicate that the phenomenon of latent inhibition is most probably still attributable to context specificity (Lovibond et al., 1984; Hall and Chanell, 1985), though this suggestion still has to be considered cautiously (Hall and Minor, 1984). The experiments of Lovibond et al. (1984) indicated that during conditioning and extinction context specificity depends upon familiarity with the environment and the associative value of the context. Their experiments 1 and 2 revealed that if the contextual features are identical, there is no question of context specificity during conditioning. Hall and Channell (1985) made the same point with respect to habituation of the orienting response (OR). However, even though environmental aspects were kept similar, it was observed that animals that received the pre-exposure treatment and conditioning in the same context showed more latent inhibition than animals that were pre-exposed and conditioned in different (albeit equal with respect to familiarity and associative value) environments (Lovibond et al., 1984, experiment 3). Thus latent inhibition might yet be caused by the pre-exposed CS entering into associations with contextual stimuli. The experiments of Hall and Channel (1985) confirm this hypothesis, in that they found that when two environments, A and B, are equally familiar to the animals, habituation does not reveal any context specific effects at all, whereas latent inhibition does. In their first experiment animals in environment A were exposed to a light stimulus which evoked an orienting response. This orienting response habituated after several presentations of the stimulus in context A. As soon as the same light

stimulus was presented in a novel environment, context B, however, a new orienting response was evoked immediately; thus, dishabituation had occurred. In a second experiment a series of new subjects, again in environment A, were exposed to repeated presentations of the light stimulus; however, these animals stayed as often in environment B, though without presentations of the light stimulus. If subsequently the light stimulus to which the animal had habituated in context A, was presented while the animal was in context B, no orienting responses were evoked, i.e. no dishabituation occurred. From this it may be concluded that habituation of the orienting response does not possess context specific properties. However, when animals from the second experiment had to learn a light-food association in context A as well as in context B, this association was established more rapidly in context B than in context A: only in context A latent inhibition was observed, which supports the idea of context specificity of latent inhibition. Thus, habituation and context specificity are apparently based on different mechanisms.
In view of this recent research, it seems plausible to assume that during pre-exposure to the CS associations are formed between the CS and contextual stimuli. Thus, it is quite possible that the presence of context-specific associations adversely affects learning processes in the shuttle box, in IC animals more so than in EC animals. Once a (say context specific) association is established, it keeps influencing the behaviour of IC animals to a larger degree than the behaviour of EC animals. Something similar could be seen in the initial perseveration of responding to a stimulus that was of relevance earlier (see chapter 5, experiment 1, 2 and 3) as well as in the sometimes better learning performance during relearning of an earlier learnt association (expriment 2). As far as once established associations are concerned, IC animals apparently do not have poorer memory than EC animals have. The formation of new associations could be based upon an increase of the α-value of the stimulus concerned. In chapter 5 we found indications that EC and IC animals do not differ with respect to increase in the α-values of stimuli. If acquisition training of a two-way active avoidance is started after CS pre-exposure, it is conceivable that, first the α-value of this contextual stimuli has to be lowered before the α-value of the CS alone contrasts sufficiently with the α-values of the contextual stimuli to allow for the formation of associations with the US. Actually, an association between the CS and contextual stimuli, formed during the pre-exposure, has to be extinguished before any new associations can be formed. In chapter 5 it was observed that IC animals are less able to inhibit high α-values; it appears that they are less able to inhibit once formed associations also.

We gained the impression that latent inhibition may be observed mainly in IC animals; particularly when training conditions are optimal (experiment 2), the phenomenon of latent inhibition does not become apparent in those animals

that have been reared in enriched environments that more closely resemble the natural conditions. Almost all studies, as far as we could determine, that concern themselves with latent inhibition per se, as well as with the effects of neural lesions and pharmacological manipulations thereon, have been using subjects reared in more or less impoverished conditions. It appears that further research, employing rats reared in enriched environments, is very much needed to explore our results further. Do animals from enriched environments establish none or almost none context specific associations with the CS, or, are these animals better equipped than IC animals to inhibit once formed associations when US presentation starts? In our opinion, the latter is the case, since in a less optimal learning procedure EC animals show some latent inhibition effects (experiment 1).

CHAPTER 7

PERSISTENCE OF BEHAVIOURAL EFFECTS, TEN MONTHS AFTER TERMINATION OF THE DIFFERENTIAL EXPERIENCE IN ENRICHED (EC) AND IMPOVERISHED (IC) ENVIRONMENTS

7.1. INTRODUCTION

The question whether behavioural efects due to a differential experience of 30 days with enriched or impoverished environments persist for a long time, has hardly ever been investigated. In most studies on effects of differential experience on brain and behaviour the animals are tested immediately or shortly after termination of the differential experience period. In a few cases EC animals were rehoused in a SC condition and tested after two months (Forgays and Reid, 1962) or a year (Denenberg et al., 1968). In both studies the animals that originated from an EC environment performed better in a Hebb-Williams maze than controls.
Brown (1971) found that some time after termination of an 80-days period in a specially visually enriched environment (which he termed an IVS) some differences could still be found in behaviour, during figure-discrimination learning, and in brain chemistry (AChE activity in the occipital cortex). The behavioural effects could be measured until 18 days after termination of the differential experience. The effects upon AChE activity, however, had disappeared within a few days. As for the persistence of the effects of differential experience on somatic variables, Bennett et al. (1974) reported the following results: the differences in AChE activity declined but could still be measured until at least 7 weeks after termination of the differential experience; during this period the original EC rats were housed in an IC condition. As far as weight differences of various parts of the brain are concerned, the weight difference of the occipital cortex lasted longest: 21 days after termination of the EC period the difference in weight was halved, and after 47 days it had disappeared. The difference in AChE activity declined at a slower rate if the EC condition had lasted 80 days than if it had lasted only 30 days. If after termination of the EC/IC period animals are tested behaviourally, the differences between EC and IC animals in brain anatomy decline more rapidly: after 25 days no differences in brain weights were observed (Krech et al., 1962, Rosenzweig et al., 1967). It is conceivable that the IC animals benefit from the stimulation presented by the formal training, or that the formal training does not offer enough stimulation for the EC subjects.
In a former experiment (chapter 3, 3.2) we found that differences in body weight had disappeared 18 days after termination of the EC condition. Thus, it appears that as far as somatic variables are concerned, the rehousing of EC animals in individual IC cages in the long run reduces or even abolishes the differences between these EC animals and IC animals in body weight and neurochemical and

neuroanatomical variables. With respect to the persistence of behavioural effects over a longer period of time, almost nothing is known. Hence, we decided to examine whether the clear behavioural effects found in the experiments 1 and 2 of chapter 6, could also be demonstrated in adult rats, 10 months after termination of the differential experience. The animals used had been reared in EC and IC environments for 40 days from weaning onwards (similarly to the subjects of the experiments 1 and 2 in chapter 6). Subsequently, the EC animals were rehoused in an IC condition. From that moment onwards all animals were kept in an IC environment until testing took place at an age of approximately 12 months. The experiment performed here is an exact replication of the first experiment in chapter 6.

7.2. EXPERIMENT 1. THE LEARNING, RELEARNING AND EXTINCTION OF A TWO-WAY ACTIVE-AVOIDANCE RESPONSE WITH AND WITHOUT CS PRE-EXPOSURE, IN ADULT ONE YEAR OLD RATS, 10 MONTHS AFTER TERMINATION OF THEIR DIFFERENTIAL EXPERIENCE IN ENRICHED (EC) AND IMPOVERISHED (IC) ENVIRONMENTS

7.2.1. METHODS

Subjects
As subjects served 40 male TMB rats (20 littermate diplets); 20 animals had originally been reared in an enriched environment, their 20 littermates came from IC environments. The animals had been kept in their respective environments during 40 days from weaning onwards. The environments used, the method of group assignment and the rearing conditions have been extensively described in chapter 2. After termination of the differential experience period all subjects were rehoused individually in macrolon cages of the IC type and kept there until the time of testing. Animals were tested at an age of approximately 360 days. 20 littermates (10 subjects from each environment) did not receive a prior exposure to the CS before training, the remaining 20 subjects were pre-exposed to the CS.

Apparatus
Shuttle box, UCS (shock) and CS (tone) were identical with those used in experiment 1 of chapter 6 (6.2.1).

Procedure
The pre-exposure procedure as well as the learning, relearning and extinction procedures were identical with those employed in experiment 1 of chapter 6 (6.2.1).

7.2.2. RESULTS

First, the results of EC and IC animals not pre-exposed to the CS will be discussed. Mean number of errors made and mean number of trials needed to reach criterion during the

phases L1, L2 and Ext, are represented in figure 7.1. Figure 7.2. shows the mean number of avoidance responses per 10 trials. One EC rat did not reach criterion during the relearning phase L2. Thus, the extinction data are based on 9 animals per group. No significant effects between the two groups were found, neither during the initial acquisition of the two-way avoidance response, nor during the relearning 24 hours later. During the extinction test, however, differences were found: animals from enriched environments made fewer errors ($F(1,8)=4.471$; $p<.05$) and needed fewer trials to reach the extinction criterion ($F(1,8)=4.124$; $p<.05$) than IC animals did.
Next the results of EC and IC animals obtained after prior exposure to the CS will be considered. Mean number of errors made and mean number of trials needed during L1, L2 and Ext are shown in figure 7.3 for both EC and IC groups. Figure 7.4 depicts the mean number of avoidance responses made per 10 trials during the three phases.
From the results it is clear that in adult rats clear differences between EC and IC groups exist as to the learning of a two-way avoidance reponse after prior exposure to the CS. EC rats make fewer errors (almost significant: $F(1,9) = 3.989$, $p<.08$) than IC animals and need significantly fewer trials to reach criterion ($F(1,9) = 6.317$, $p<.05$). Two IC rats did not reach criterion during the acquisition phase L1; thus, the results from the relearning (L2) and extinction (Ext) phases are based upon eight IC animals and their eight littermates.
During relearning and extinction on the second day of testing no differences between EC and IC groups were found with respect to number of errors made and number of trials needed. During extinction, the directions of the differences are the same as those observed in experiment 1 in chapter 6. Just as in experiment 2 of chapter 6, it is again found that pre-exposure to the CS does not affect the acquisition of a two-way active avoidance response in EC animals, though it does so in IC animals. IC animals do not acquire the two-way active avoidance response after CS pre-exposure as well as they do without CS pre-exposure; this is evident as to the number of errors made (Mann-Whitney U test, $U = 8$, $p<.001$) as well as to the number of trials needed ($U = 9$, $p<.001$).

7.3. DISCUSSION

This experiment demonstrates that, even a longtime after termination of a differential experience period of 40 days immediately after weaning, behaviour patterns may occur that must be attributed to this differential experience. The pattern of behavioural differences observed in this experiment is almost identical with the findings for rats that have been tested immediatly after termination of their housing in the respective environments (chapter 6, experiment 1 and 2). It is found here that 10 months after termination of the differential housing during 40 days in EC and IC environments, adult rats do not differ in their acquisition of a two-way avoidance response in the shuttle

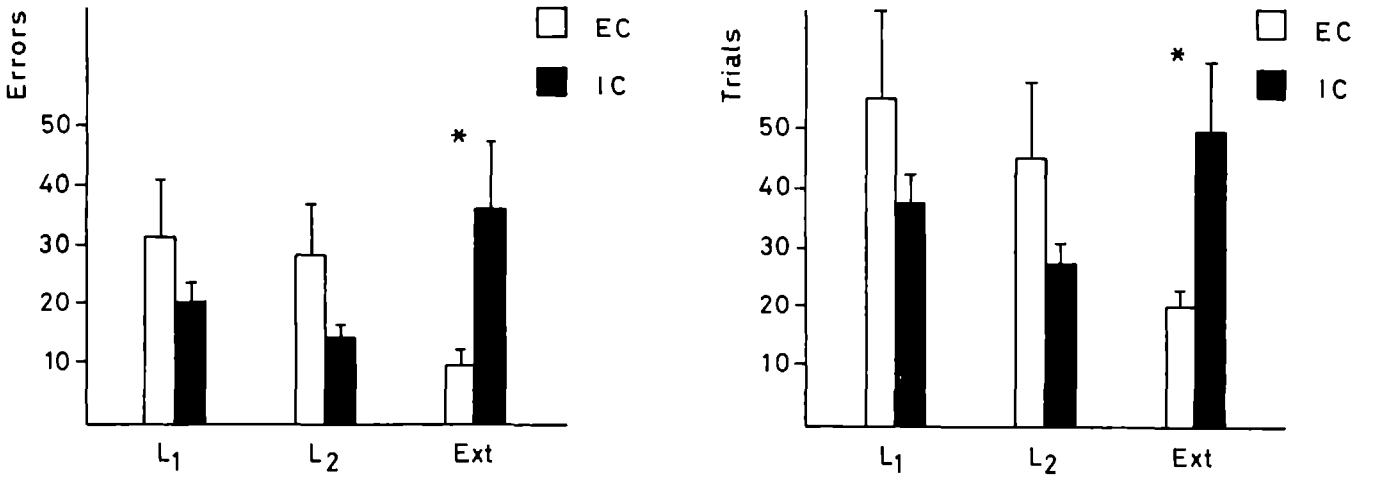

Figure 7.1. Mean number of errors (± SEM) and mean number of trials (± SEM) for EC and IC rats, 10 months after termination of the differential experience, on the acquisition of a two-way active avoidance problem (L1), and on relearning (L2) and extinction (Ext) of the problem, without pre-exposure of the CS.
*$p < .05$

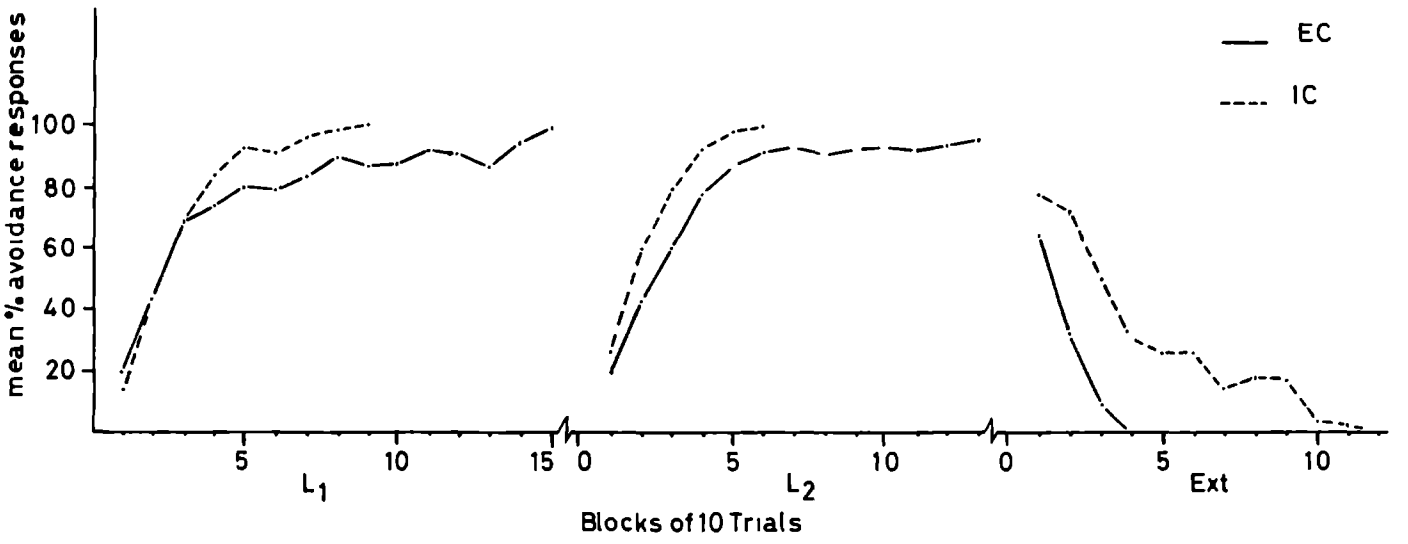

Figure 7.2. Mean percentage of avoidance responses over blocks of 10 trials for EC and IC rats, 10 months after termination of the differential experience, on the acquisition of a two-way active avoidance problem (L1), and on relearning (L2) and extinction (Ext) of the problem, without pre-exposure of the CS.

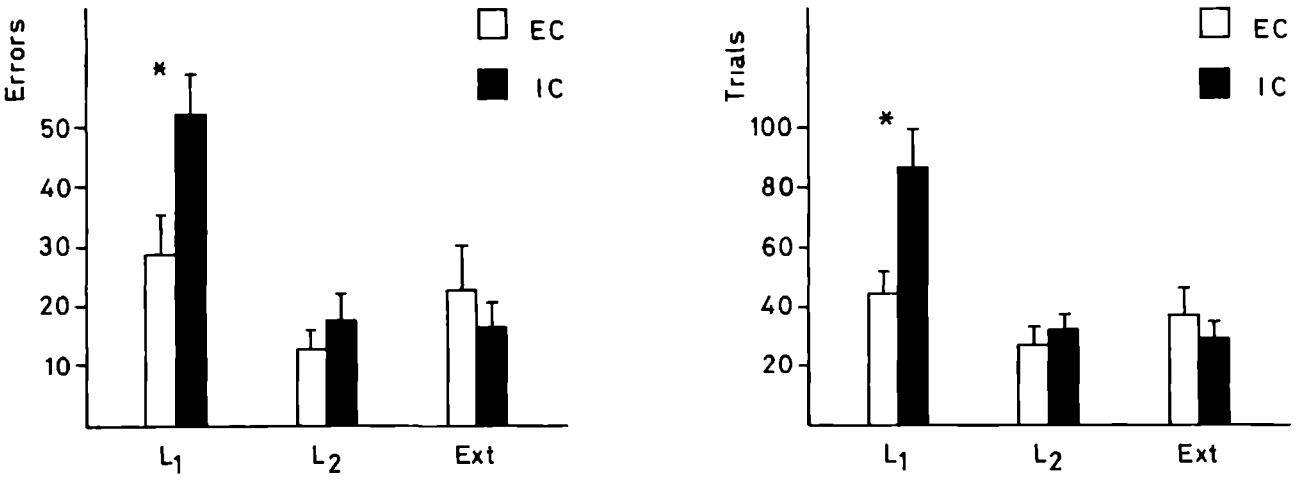

Figure 7.3. Mean number of errors (± SEM) and mean number of trials (± SEM) for EC and IC rats, 10 months after termination of the differential experience, on the acquisition of a two-way active avoidance problem (L1), and on relearning (L2) and extinction (Ext) of the problem, with pre-exposure of the CS.
*$p < 05$

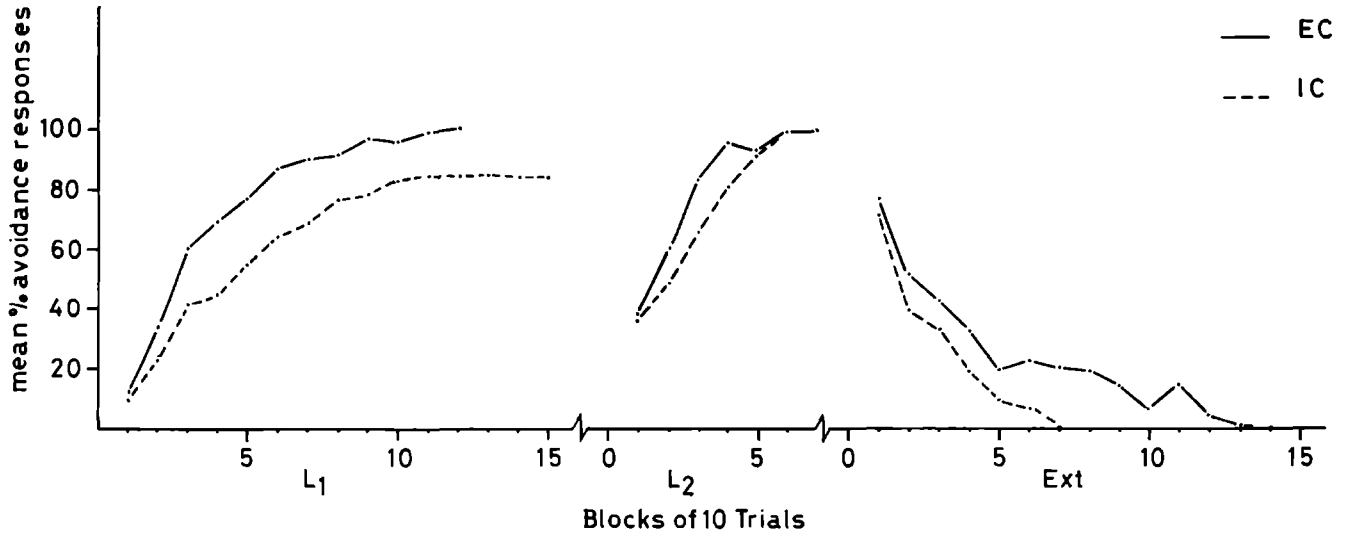

Figure 7.4. Mean percentage of avoidance responses over blocks of 10 trials for EC and IC rats, 10 months after termination of the differential experience, on the acquisition of a two-way active avoidance problem (L1), and on relearning (L2) and extinction (Ext) of the problem, with pre-exposure of the CS.

box. This was observed also in experiments 1 and 2 in chapter 6. The animals of the latter two experiments were, however, tested three days after termination of the differential housing. Though the directions in which relearn scores tend to go in the present experiment are similar to those observed in the experiments 1 and 2 in chapter 6, in the present experiment no significant differences were found, whereas in experiment 2 of chapter 6 significances were reached. Differences between EC an IC animals during extinction were significant. IC rats extinguished significantly slower than EC animals, though only if they had not received CS pre-exposure prior to the initial acquisition of the response.
This experiment also demonstrates that after CS pre-exposure adult rats, originally reared in an IC environment, do not acquire the two-way active avoidance response as easily as adult rats reared in EC environments. This acquisition difference was also observed in the experiments 1 and 2 in chapter 6, but then the latter rats were tested immediatly after termination of the environmental exposure. The difference in acquisition found for EC and IC animals after prior exposure to the CS again appears to be attributable to the IC subjects performing poorer after CS pre-exposure, whereas the same CS pre-exposure does not seem to affect the learning performance of the EC group. Thus, in general it can be maintained that even a long time after termination of housing in environments with varying stimulus complexities, behavioural effects may be observed that are similar to those found immediatly after termination of the differential housing conditions. It may be true that effects on brain anatomy and brain chemistry apparently disappear rather fast (Brown, 1971, Bennett et al., 1974), our experiments represent evidence that the behavioural effects are more persistent.

CHAPTER 8

SUMMARY

The aim of this dissertation has been to conduct research into effects of differential experience induced by housing animals in environments of varying stimulus complexities upon behaviour.

Chapter 1 represents a general introduction into the subject of this thesis. In the first part of this chapter a short survey of the field of research is given and the results of studies concerning the effects of rearing in environments of varying stimulus complexities (also called differential experience) on brain and behaviour are reviewed. These studies have been conducted largely by a group of scientists of the University of California, Berkeley, California, U.S.A. (Bennett, Diamond, Krech and Rosenzweig). Their studies concentrated mainly upon the effects of differential experience on brain chemistry and brain anatomy. Behavioural effects have not been studied extensively by this group. Behavioural effects have been studied, though, by other scientists. However, the many different environments used, the differences in the thechniques of behavioural testing etcetera render them extremely difficult to survey.
In the second part of chapter 1 some particular effects on neurochemical and behavioural variables are discussed. From this we developed the idea that differential experience, through rearing in environments with varying stimulus complexities, possibly affects the functioning of the cholinergic system. After having discussed the relationship between the cholinergic system and behaviour, we formulated the hypothesis that effects of differential experience on behaviour are specifically related to the degree of efficiency in stimulus selection, particularly with respect to inhibition of irrelevant stimuli, resulting in effects on behavioural inhibition.

Departing from this hypothesis experiments were designed to examine effects of differential experience on the efficiency of stimulus selection. These experiments are concerned with habituation (chapter 4), discrimination and reversal learning (chapter 5), and latent inhibition (chapter 6).

Chapter 2 describes the environments of varying stimulus complexities we have used to induce differential experience. Also described here are the general procedures concerning group assignment and living conditions in the respective environments.

Before starting our research into the effects of differential experience on the efficiency of stimulus selection, we first planned to verify whether housing in the environments we were going to use, produced the same effects on the weights of various parts of the brain as those frequently reported by the Berkeley group. Chapter 3

describes this experiment. Our results almost exactly replicate the Berkeley findings. Thus, it may be concluded that the effects on the brain induced by our environments and those induced by the environments used by the Berkeley group, were identical.
The Berkeley group concentrated on an increasingly closer analysis of the neurochemical and neuroanatomical effects. In contrast, we aimed to further analyse the behavioural effects.
The second experiment of chapter 3 investigated whether social stimulation versus social isolation represented sufficient differential experience to result in comparable effects upon the weight of various parts of the brain. The evidence obtained indicated that indeed this was so. Based on the results of this experiment as well as on recent studies by the Berkeley group we concluded that the search for one factor in the various environments differing in complexity (e.g. size of the cage), which might possibly explain all the effects, is not so important. Instead, it seems important to concentrate on the amount of stimulation and the ways of coping with this stimulation (particularly, active interaction), since this appears to be a crucial factor in the development of effects on brain and behaviour, more so than the type of stimulation per se (e.g. animate versus inanimate). Further, the results of the second experiment enabled us also to involve the results of studies that investigated the effects of social isolation versus group housing on behaviour.

Chapter 4 examines effects of differential experience on habituation. A main feature of experiemtns concerning habituation is that the animals are confronted with an unfamiliar novel situation, which after certain amount of time loses its novelty and relevance.
In four experiments EC and IC animals were confronted with an unchanging stimulus situation, independent of their behaviour. The first three experiments explored eventual changes in locomotor activity in the open field. It was found that during a forced exposure to the open field (experiment 1) both EC and IC animals initially started with a comparatively high level of locomotor activity that decreased in the course of time. This decline proceeded more rapidly in the EC group: EC rats showed a faster habituation compared with their IC littermates. During two tests in which the animals had free entrance to the open field (experiments 2 and 3), it appeared that both the IC and the EC group started with a rather low level of locomotor activity in the open field; activity increased in the course of time. It was found that EC animals started locomotor activity in the open field sooner than IC animals did. A difference in the rate of increase was not observed, however.The fourth experiment of this chapter studied the decline of startle responses during repeated presentations of loud tones. It was found that EC and IC animals did not differ as to the habituation of a startle response.
Interestingly, it has been found that an inhibition of the activity of the cholinergic system abolishes the decrease in

locomotor activity in the open field, but has no effect on the attenuation of the startle response (Williams et al., 1974).

In chapter 5 a number of experiments are reported that investigated effects of differential experience on discrimination and reversal learning. A maze was used in which spatial as well as visual discriminative stimuli could be introduced. During acquisition of the discrimination response the amount of stimulation presented to the animal was manipulated. Reversal learning consisted of intradimensional and extradimensional shifts. Discrimination and reversal learning were analysed in terms of 'hypothesis' behaviour (as described by Krechevsky, 1932a and b) and Mackintosh's theory (Mackintosh, 1973, 1975) on the functioning of stimulus selection processes.
It appeared that in the presence of irrelevant stimulation IC animals showed poorer learning performance than EC rats. When irrelevant stimulation was absent, no such differences were observed. It was also found that during reversal learning IC animals initially made more errors than EC animals. This is caused by the fact that IC animals keep responding longer to the stimulus that was relevant before. Both results are strong evidence that IC animals have a less efficient stimulus selection system, in that they are less able to suppress irrelevant stimuli. This dysfunction might be explained by assuming that IC animals do not very well reduce the α-values of stimuli correlated with nonreinforcement.
The more often the animals were confronted with reversals, the more the differences between EC and IC animals declined. However, this was true only if the reversals were processed in the same analyzer.
The rat strain we have used (TMB) has a preference for solving discrimination problems through spatial hypotheses; this is probably caused by a genetically determined higher α-value for spatial hypotheses as compared with brightness hypotheses. It was found that during acquisition and reversal of the brightness discrimination IC animals return to this preference more often than EC animals do. Thus, again it seemed that the stimulus selection processes functioned less optimally in the IC subjects, as compared with EC animals.

Chapter 6 is devoted to a number of studies of the influence of differential experience upon two-way active avoidance learning in a shuttle box, with or without prior exposure to the CS. Generally, CS pre-exposure retards acquisition of a learning task, which effect is called 'latent inhibition'. Initially, latent inhibition was thought to a result of diminuation of the signal-value of the CS. Recently, strong indications have been found that latent inhibition is a consequence of associations formed between the CS and context-specific stimuli (Lovibond et al., 1984; Hall and Channell, 1985).
It was found that in the absence of CS pre-exposure EC and IC animals did not differ in acquisition of the active

avoidance response. Following CS pre-exposure, however, IC animals showed poorer learning performance than EC animals. This result was replicated. An earlier experiment (chapter 4, experiment 4) indicated that EC and IC animals habituate as fast to a repeatedly presented tone. Thus, the difference in learning rate found here after CS pre-exposure, can not be attributed to a slower habituation to the CS in IC animals. IC animals apparently are more hampered by the associations established between the CS and contextual stimuli during the pre-exposure. Hence, during acquisition of the two-way active avoidance response they are less able to inhibit these associations formed previously, which results in the CS entering less easily into new associations with the US.
Moreover, indications were found that "latent inhibition" may be observed more easily in IC animals and hardly at all in EC animals.
A third result from this series of experiments is that IC animals relearn the avoidance response sooner than EC animals do. Thus, it may be concluded that the memory of once formed associations in IC animals is no less than that in EC animals. The results of these experiments, finally, demonstrate that EC and IC animals do not differ as to the extinction of an acquired avoidance response.

Chapter 7 concentrates on research into the persistence of the behavioural effects due to differential experience. 10 months after termination of the differential experiences with environments of varying stimulus complexities, effects upon the acquisition of a two-way avoidance response, after prior exposure to the CS, are found which are almost identical with the effects obtained immediately after termination of the differential experience conditions. This indicates that these behavioural effects are comparatively "permanent" during a long time after termination of the differential experience.

When we look at the cerebral differences between EC and IC animals now, it strikes us that the cortex, (particularly the occipital area) of EC animals is clearly more developed than that of IC animals (chapter 1; chapter 3, experiments 1 and 2). An intriguing possibility, based on data from Fessard and Szabo (1951), Weitzman (1963) and Douglas (1967), was suggested by Vossen (1968), the purport of which is that the discriminating capacity of the limbic system decreases due to deficits in one or more cortex areas, which results in a reduced capacity to organize sensory input in terms of figure and background. If we consider the results of the behavioural experiments in totality, we find that EC and IC animals differ above all things in the rate at which behavioural changes come about in response to unchanging or changing stimulus situations. There is no clear evidence to warrant the assumption that IC animals have a memory system that does not function so well. In complex stimulus situations IC animals are less able than EC animals to quickly distinguish between relevant and irrelevant stimuli,

because they are less able to inhibit irrelevant stimuli by lowering the α-values of these stimuli when they are correlated with nonreinforcement. In a simple situation these animals have no problems. IC animals preserve responses to originally relevant stimuli longer, after these have become irrelevant in the context of behavioural adaption to the stimulus situation. The reduction of the α-value, and hence the transition into irrelevance (during habituation, discrimination and reversal learning and latent inhibition) does not proceed in the IC animals as fast as in EC animals.

It is conceivable that certain neuroanatomical structures play an important part in the increase and decrease of the α-values. The hippocampus, particularly, appears to have an important role in the reduction of α-values of stimuli, when these are correlated with nonreinforcement (Douglas and Pribram, 1966, 1969; Pribram et al., 1969). Interestingly, their is almost no brain structure known to be more 'cholinergic' than the hippocampus (Douglas, 1972).In rats it appears that the hippocampus becomes functional at an age of approximately 25 days (Jones, 1980), which is the age at which the animals are usually weaned and the differential experience period starts. It has been found that precisely isolation during this period (25th to 55th day) produces irreversible effects, whereas the effects induced by isolation during other periods are largely reversible (Krech et al., 1962; Einon and Morgan, 1977). It could be that the period immediately after weaning constitutes a critical period for the development of an optimal functioning of the hippocampal region, and that stimulus deprivation and too little experience cause a permanent deficency in this area.

Het doel van dit proefschrift was, onderzoek te doen naar de effekten van differentiał experience te gevolge van een verblijf in omgevingen met verschillende stimuluskomplexiteiten op gedrag.

Hoofdstuk 1 bevat een algemene inleiding in het onderwerp van deze thesis. In het eerste deel van dit hoofdstuk wordt een beknopt overzicht gegeven van het veld van onderzoek en van de resultaten van experimenten betreffende de effekten van het verblijf in omgevingen met verschillende stimulus kompexiteiten (differentiał experience genoemd) op hersenen en gedrag. Deze experimenten zijn voor een groot deel uitgevoerd door een groep onderzoekers van de University of California, Berkeley, California, U.S.A. (Bennett, Diamond, Krech en Rosenzweig). Hun onderzoek richtte zich vooral op effekten van differentiał experience op neurochemische en neuroanatomische variabelen. Onderzoek naar effekten op gedrag is door hen weinig uitgevoerd. Effekten op gedrag zijn wel door andere onderzoekers ter hand genomen maar de vele verschillende omgevingen, de verschillen in techniek van gedragsmetingen etcetera maken een algeheel overzicht hiervan bijzonder moeilijk.
In het tweede deel van dit hoofdstuk worden een aantal gegevens betreffende effekten op neurochemische en gedragsvariabelen besproken. Van daaruit komen wij tot de veronderstelling, dat differentiał experience, middels het opgroeien in omgevingen met verschillende stimulus komplexiteiten, mogelijk een effekt heeft op het funktioneren van het cholinerge systeem. Vanuit een bespreking van de relatie tusssen het funktioneren van het cholinerge systeem en gedrag komen wij vervolgens tot de hypothese, dat effekten van differentiał experience op gedrag specifiek betrekking hebben op de mate van efficientheid van stimulus selectie, met name wat betreft de inhibitie van irrelevante stimuli, en de daaruit resulterende effekten op gedragsinhibitie.

Uitgaande van deze hypothese werden een aantal experimenten ontworpen welke tot doel hadden effekten van differentiał experience op de efficientheid van stimulus selectie te onderzoeken. Deze experimenten betreffen onderzoek naar habituatie (hoofdstuk 4), discriminatie en reversal leren (hoofdstuk 5), en latent inhibition (hoofdstuk 6).

Hoofdstuk 2 omvat een overzicht van de omgevingen met verschillende stimulus komplexiteiten die door ons werden gebruikt ten einde een differentiał experience mogelijk te maken. Tevens wordt in dit hoofdstuk beschreven op welke manier de indeling en verblijf in deze omgevingen plaats vond.

Alvorens te starten met het onderzoek naar effekten van differentiał experience op de efficientheid van stimulus selectie, wilden wij eerst verifieren of een verblijf in de

door ons te gebruiken omgevingen dezelfde effekten op het gewicht van verschillende hersendelen tot gevolg had als die welke veelvuldig door de Berkeley groep zijn gepubliceerd. Hoofdstuk 3 omvat de beschrijving van dit experiment. Het bleek, dat onze resultaten een vrijwel exacte replicatie waren van de resultaten van de Berkeley groep. Daaruit kan gekonkludeerd worden, dat de omgevingen die door ons gebruikt worden en de omgevingen die door de Berkeley groep worden gebruikt, vergelijkbare effekten op de hersenen tot gevolg hebben. De Berkeley groep heeft zich voornamelijk verdiept in een steeds verdergaande analyse van de neurochemische en neuroanatomische effekten. Onze opzet was tot een verdere analyse van de gedragseffekten te geraken.
Het tweede experiment dat in hoofdstuk 3 wordt besproken had tot doel na te gaan of sociale stimulatie versus sociale isolatie voldoende differential experience vormt om vergelijkbare effekten op het gewicht van verschillende hersendelen tot gevolg te hebben. Dit bleek inderdaad het geval te zijn. Vanuit dit onderzoek, alsmede vanuit recente onderzoekingen van de Berkeley groep komen wij tot de veronderstelling, dat het zoeken naar een mogelijke alles-verklarende faktor (bv. kooigrootte) in de van elkaar in stimuluskomplexiteit verschillende omgevingen van minder belang is. Veeleer is het van belang de hoeveelheid stimulatie en de manier van omgaan met deze stimulatie (met name aktieve interaktie) als maatstaf te gebruiken. Het is dit dat de bepalende faktor vormt in het ontstaan van hersen- en gedragseffekten en dus niet het soort stimulatie op zich (bv. inanimate vs. animate). De resultaten van dit tweede experimant openden voor ons tevens de weg om de resultaten van de in de literatuur vermelde experimenten betreffende de effekten van sociale isolatie versus group housing op gedrag in ons onderzoek te betrekken.

Hoofdstuk 4 gaat over onderzoek naar effekten van differential experience op habituatie. Kenmerkend bij habituatie experimenten is dat stimuli aanvankelijk nieuwheid en relevantie kenmerken bezitten, welke kenmerken na verloop van tijd afnemen.
In een viertal experimenten werden de EC en IC dieren, onafhankelijk van hun gedrag, met een gelijkblijvende stimulus situatie gekonfronteerd. De eerste drie experimenten richtten zich op onderzoek naar de verandering van locomotor aktiviteit in het open veld. Het bleek, dat bij een gedwongen verblijf in het open veld (experiement 1), EC en IC dieren beide met een relatief hoge lokomotor aktiviteit begonnen, welke afnam in funktie van de tijd. De afname bleek sneller te verlopen bij de EC dieren: EC dieren habitueren hier sneller dan hun IC nestgenoten. Bij een vrije toegang tot een open veld (experimenten 2 en 3) bleken EC en IC dieren beide met een relatief lage lokomotor aktiviteit in dit open veld te beginnen; deze nam toe in funktie van de tijd. Het bleek, dat EC dieren eerder begonnen met lokomotor aktiviteit in het open veld dan IC dieren. Een verschil in de snelheid van toename werd niet gevonden. Het vierde experiment in dit hoofdstuk had betrekking op de afname van schrikreacties

(startle-responses) bij een herhaald aanbieden van luide tonen. Het bleek, dat EC en IC dieren niet van elkaar verschilden in de habituatie van de startle-response.
Interessant is nu dat gevonden is dat een afremming van de aktiviteit van het cholinerge systeem enerzijds de afname van locomotor aktiviteit in het open veld te niet doet, maar anderzijds geen effekt heeft op de afname van de startle response (Williams et al., 1974).

In hoofdstuk 5 wordt verslag gedaan van een aantal experimenten welke tot doel hadden effekten van differential experience op discriminatie en reversal leren te onderzoeken. Hierbij werd gebruik gemaakt van een doolhof, waarin naast ruimtelijke ook visuele discriminatieve stimuli konden worden geintroduceerd. Bij het aanleren van een discriminatie kon zo de hoeveelheid irrelevante stimulatie worden gemanipuleerd. Het reversal leren had betrekking op zowel intradimensionele als extradimensionele shifts. Het discriminatie en reversal leren werd geanalyserd in termen van 'hypothese' gedrag (zoals beschreven door Krechevsky, 1932a en b) alsmede in termen van de theorie van Mackintosh (1973, 1975) omtrent het funtioneren van stimulus selectie processen.
Het bleek, dat IC dieren bij het aanleren van een discriminatie probleem slechtere prestaties leverden dan EC dieren in aanwezigheid van irrelevante stimulatie. Bij de afwezigheid van de irrelevante stimulatie was er geen verschil in het aanleergedrag tussen de IC en EC dieren. Voorts werd gevonden, dat IC dieren bij reversal leren aanvankelijk meer fouten maken dan de EC dieren. Dit wordt veroorzaakt doordat de IC dieren langer blijven responderen op de voorheen relevante stimulus. Beide gegevens geven ons sterke aanwijzingen, dat IC dieren een minder efficient stimulus selectie systeem bezitten, en wel doordat zij minder goed in staat zijn irrelevante stimuli te inhiberen. Deze dysfunktie lijkt te worden veroorzaakt doordat de IC dieren minder goed de α-waarden van die stimuli verlagen, die gecorreleerd worden met non-reinforcement.
Naarmate de dieren vaker met reversals werden gekonfronteerd, ging dit verschil tussen de EC en IC dieren verdwijnen, echter alleen als het reversals betrof in dezelfde analyzer.
De door ons gebruikte rattenstam (TMB) heeft een voorkeur voor het oplossen van discriminatie problemen door middel van ruimtelijke hypothesen, hetgeen veroorzaakt zou kunnen worden door een -genetisch bepaalde- hogere α-waarde voor ruimtelijke stimuli dan voor helderheids stimuli. Het bleek nu, dat bij het leren en reversal leren van helderheidsdiscriminaties IC dieren meer terugvallen op deze voorkeur dan EC dieren. Ook zo bleek dus de stimulus selectie bij IC dieren minder optimaal te verlopen dan die bij EC dieren.

Hoofdstuk 6 is gewijd aan een aantal onderzoekingen naar de invloed van differential experience op two-way active avoidance leren in de shuttle-box, met en zonder pre-exposure van de CS. Pre-exposure van de CS heeft in het

algemeen minder goede leerprestaties tot gevolg. Dit phenomeen wordt 'latent inhibition' genoemd. Aanvankelijk werd latent inhibition gezien als een gevolg van een afname in signaal waarde van de CS. Recent zijn er sterke aanwijzingen gevonden dat latent inhibition een gevolg is van het ontstaan van associaties tussen de CS en contextuele stimuli (Lovibond et al., 1984; Hall en Channell, 1985).
Het bleek, dat in afwezigheid van pre-exposure van de CS, EC en IC dieren niet van elkaar verschillen in het aanleren van een two-way active avoidance response. IC dieren leerden deze avoidance response echter veel slechter in vergelijking met EC dieren na pre-exposure van de CS. Dit gegeven kon worden gerepliceerd. Uit een eerder uitgevoerd experiment (hoofdstuk 4, experiment 4) is gebleken, dat EC en IC dieren even snel habitueren aan een herhaald aangeboden pieptoon. Het verschil in leersnelheid na pre-exposure van de CS is dus niet te wijten aan een tragere habituatie aan de CS bij de IC dieren. IC dieren hebben meer last van tijdens de pre-exposure gevormde associaties tussen de CS en contextuele stimuli. Tijdens acquisitie van het two-way active avoidance leren lijken zij minder goed in staat om de tijdens de pre-exposure gevormde associaties tussen de CS en contextuele stimuli te inhiberen, waardoor de CS moeilijker een nieuwe associatie aangaat met de US.
Voorts zijn er aanwijzingen gevonden dat 'latent inhibition' een effekt is wat vooral zichtbaar blijkt te zijn bij dieren uit een IC konditie en niet of nauwelijks bij dieren uit een EC konditie.
Een derde gegeven dat uit de experimenten naar voren komt, is dat IC dieren de avoidance response sneller herleren dan de EC dieren. Het geheugen voor eenmaal gevormde associaties lijkt bij IC dieren dus zeker niet slechter te zijn dan bij EC dieren. De resultaten van de experimenten uit dit hoofdstuk wijzen verder uit, dat EC en IC dieren niet van elkaar verschillen in de extinctie van de aangeleerde avoidance response.

Hoofdstuk 7 is gewijd aan onderzoek naar het aanblijven van de effekten op gedrag die ten gevolge van differential experience zijn ontstaan. Het bleek, dat 10 maanden na beeindiging van de differential experience in omgevingen met verschillende stimulus komplexiteiten, er identieke effekten op het aanleren van een two-way avoidance response, na pre-exposure van de CS, gevonden werden, als die welke direkt na beeindiging van dit verblijf aanwezig waren. Dit betekent, dat deze effekten op gedrag relatief 'permanent' aanwezig blijven, lange tijd na beeindiging van de differential experience.

Bezien we nu de cerebrale verschillen tussen EC en IC dieren, dan valt op dat de cortex (met name in het occipitale gebied) van EC dieren duidelijk meer ontwikkeld, uitgegroeid is dan die van IC dieren (hoofdstuk 1; hoofdstuk 3, experimenten 1 en 2). Interessant is nu de suggestie van Vossen (1968), op grond van bevindingen van Fessard en Szabo (1951), Weitzman (1963) en Douglas (1967), dat het differentierend vermogen van het limbisch systeem

vermindert, als gevolg van uitval van een of meer cortexarealen, hetgeen tot uiting komt in een afname van het vermogen de sensorische input te organiseren in termen van figuur en achtergrond. Bezien we namenlijk de resultaten van de gedrags-experimenten in totaliteit, dan zien we dat EC en IC dieren vooral verschillen in snelheid, waarmee gedragsveranderingen ten aanzien van gelijkblijvende of veranderende stimulus situaties worden uitgevoerd. Er zijn geen aanwijzingen om te veronderstellen dat IC dieren een minder goed werkend geheugen zouden hebben. IC dieren kunnen in een komplexe stimulus situatie minder snel dan EC dieren een onderscheid maken tussen relevante en irrelevante stimuli, doordat zij minder goed in staat zijn irrelevante stimuli te inhiberen via verlaging van de α-waarde van die stimuli, wanneer die gecorreleerd worden met non-reinforcement. In een eenvoudige stimulus situatie is er in leervermogen dan ook weinig tot geen verschil. Verder is duidelijk geworden, dat IC dieren langer blijven responderen op oorspronkelijk relevante stimuli, wanneer deze in het kader van gedragsaanpassing aan de stimulus situatie niet meer relevant zijn, hun relevantie verliezen. De afname van de α-waarde en aldus de overgang naar irrelevantie (bij habituatie, discriminatie en reversal leren en latent inhibition) verloopt minder snel bij IC dieren.
Het is voorstelbaar, dat bij de toename en afname van de α-waarden van stimuli bepaalde neuroanatomische strukturen een belangrijke rol spelen. Met name de hippocampus lijkt een belangrijke rol te spelen in de afname van de α-waarden van stimuli, wanneer die worden gecorreleerd met non-reinforcement (Douglas en Pribram, 1966, 1969; Pribram et al., 1969). Interessant is, dat er nauwgelijks een hersengebied te vinden is dat zo 'cholinerg' is als de hippocampus (Douglas, 1972). De hippocampus blijkt bij ratten op een leeftijd rond de 25e dag funktioneel te worden (Jones, 1980), dus rond de leeftijd waarop gewoonlijk gespeend wordt en begonnen wordt met de differential experience periode. Het is nu gebleken, dat juist isolatie gedurende deze periode (25e tot 55e dag) irreversibele effekten kan veroorzaken terwijl isolatie tijdens andere periodes reversibele gedragseffekten laat zien (Krech et al., 1962; Einon en Morgan, 1977). Mogelijk dat de periode vlak na het spenen bij ratten een kritische periode vormt om tot een optimale werking te komen van dit hippocampale gebied, en dat bij stimulusdeprivatie, een te geringe experience, dit gebied blijvend zwak funktioneert.

Ackil, J.E., Mellgren, R.L., Halgren, C.R. and Frommer, G.P. (1969). Effects of CS preexposure on avoidance learning in rats with hippocampal lesions. Journal of Comparative and Physiological Psychology, 69, 739-747.

Aitken, P.P. (1974). Early experience, emotionality, and exploration in the rat: a critique of Whimbey and Denenberg's Hypothesis. Developmental Psychobiology, 7, 129-134.

Asratyan, E.A. (1965). Compensatory adaptation, reflex activity and the brain. Oxford: Pergamon Press.

Aulich, D. (1976). Escape versus exploratory activity: an interpretation of rats' behavior in the open field and a light-dark preference test. Behavioral Processes, 1, 153-164.

Baenninger, L.P. (1967). Comparison of behavioral development in socially isolated and grouped rats. Animal Behaviour, 15, 312-323.

Balaz, M.A., Capra, S., Hartl, P. and Miller, R.R. (1981). Contextual potentiation of acquired behavior after devaluing direct context - US associations. Learning and Motivation, 12, 383-397.

Bekoff, M. and Fox, M.W. (1972). Postnatal neural ontogony: environment-dependent and/or environment-expectant? Developmental Psychobiology, 5, 323-341.

Bennett, E.L., Diamond, M.C., Krech, D. and Rosenzweig, M.R. (1964). Chemical and anatomical plasticity of brain. Science, 146, 610-619.

Bennett, E.L., Rosenzweig, M.R. and Diamond, M.C. (1970). Time courses of effects of differential experience on brain measures and behavior of rats. In: W.L. Byrne (Ed.), Molecular approaches to learning and memory (pp. 55-89). New York: Academic Press.

Bennett, E.L., Rosenzweig, M.R. and Diamond, M.C. (1974). Effects of successive environments on brain measures. Physiology and Behavior, 12, 621-631.

Bennett, E.L. (1976). Cerebral effects of differential experience and training. In: M.R. Rosenzweig and E.L. Bennett (Eds.), Neural Mechanisms of learning and memory (pp. 279-289). Cambridge: The MIT Press.

Blanchard, R.J., Kelley, M.J. and Blanchard, D.C. (1974). Defensive reactions and exploratory behavior in rats. Journal of Comparative and Physiological Psychology, 87, 1129-1133.

Bouton, M.E. and Bolles, R.C. (1979). Contextual control of the extinction of conditioned fear. Learning and Motivation, 10, 445-466.

Bower, G.H., Starr, R. and Lazarovitz, L. (1965). Amount of response-produced change in the CS and avoidance learning. Journal of Comparative and Physiological Psychology, 59, 13-17.

Bronstein, P.M., Neiman, H., Wolkoff, D. and Levine, M.J. (1974). The development of habituation in the rat. Animal Learning and Behavior, 2, 92-96.

Brown, C.P. (1971). Cholinergic activity in rats following enriched stimulation and training: direction and duration of effects. Journal of Comparative and Physiological Psychology, 75, 408-416.

Brown, K. and Warburton, D.M. (1971). Attenuation of stimulus sensibility by scopolamine. Psychonomic Science, 22, 297-298.

Calhoun, K.S., Prewett, M.J., Douglas Peters, R. and Adams, H.E. (1975). Factors in the modification by isolation of electroconvulsive shock-produced retrograde amnesia in the rat. Journal of Comparative and Physiological Psychology, 88, 373-377.

Campbell, B.A., Lyttle, L.D. and Fibiger, H.C. (1969). Ontogeny of adrenergic and cholinergic inhibition in the rat. Science, 166, 637-638.

Carlton, P.L. (1963). Cholinergic mechanisms in the control of behavior by the brain. Psychological Review, 70, 19-39.

Carlton, P.L. (1968). Brain acetylcholine and habituation. In: P.B. Bradley and M. Fink (Eds.), Anticholinergic drugs and brain function in animals and man (Progress in Brain Research, Vol. 28, pp. 48-60). Amsterdam: Elsevier.

Carlton, P.L. (1969). Brain-acetylcholine and inhibition. In J.T. Tapp (Ed.), Reinforcement and Behavior (pp. 287-327). New York: Academic Press.

Channell, S. and Hall, G. (1983). Contextual effects in latent inhibition with an appetitive conditioning procedure. Animal Learning and Behavior, 11, 67-74.

Cheal, M.L. (1981). Scopolamine disrupts maintenance of attention rather than memory processes. Behavioral and Neural Biology, 33, 163-187.

Collins, R.A. (1970). Experimental modification of brain weight and behavior in mice: an enrichment study. Developmental Psychobiology, 3, 145-155.

Coyle, I.R. and Singer, G. (1975). The interaction of post-weaning housing conditions and prenatal drug effects on behavior. Psychopharmacologia, 41, 237-244.

Cragg, B.G. (1969). The effects of vision and dark-rearing on the size and density of synapses in the lateral geniculate nucleus measured by electron microscopy. Brain Research, 13, 53-67.

Cragg, B.G. (1975). The development of synapses in kitten visual cortex during visual deprivation. Experimental Neurology, 46, 445-451.

Creutzfeldt, O.D. and Heggelund, P. (1975). Neural plasticity in visual cortex of adult cats after exposure to visual patterns. Science, 188, 1025-1027.

Dalrymple-Alford, J.C. and Benton, D. (1981a). The effect of social isolation of the rat on open field activity and emergence. Behavioral Processes, 6, 283-290.

Dalrymple-Alford, J.C. and Benton, D. (1981b). Activity differences of individually and group-housed male and female rats. Animal Learning and Behavior, 9, 50-55.

Dalrymple-Alford, J.C. and Benton, D. (1984). Behavioral inhibition and the age at social isolation in rats. Quarterly Journal of Experimental Psychology, 36B, 39-51.

Davis, M. (1972). Differential retention of sensitization and habituation of the startle response in the rat. Journal of Comparative and Physiological Psychology, 78, 260-267.

DeFeudis, F.V. (1975). Cerebral biochemical and pharmacological changes in differentially housed mice. In: W.B. Essman and L. Valzelli (Eds.), Current Developments in Psychopharmacology (Vol. 1, pp. 143-201). New York: Spectrum Publications Inc..

DeFeudis, F.V. (1979). Environment and central neurotransmitters in relation to learning, memory and behavior. Genetic Pharmacology, 10, 281-286.

Denenberg, V.H. and Morton, J.R.C. (1962). Effects of environmental complexity and social groupings upon modification of emotional behavior. Journal of Comparative and Physiological Psychology, 55, 242-246.

Denenberg, V.H. and Grota, L.J. (1964). Social-seeking and novelty-seeking behavior as a function of differential rearing histories. Journal of Abnormal and Social Psychology, 69, 453-456.

Denenberg, V.H., Woodcock, J.M. and Rosenberg, K.M. (1968). Long-term effects of preweaning and postweaning free-environment experience on rats problem-solving behavior. Journal of Comparative and Physiological Psychology, 66, 533-535.

Denenberg, V.H. (1969). Open-field behavior in the rat: what does it mean? Annals New York Academy of Sciences, 852-859.

Deutsch, J.A. (1966). Substrates of learning and memory. Dis. Nerv. Sys., 27, 20-24.

Deutsch, J.A. (1969). The physiological basis of memory. Annual Review of Psychology, 20, 85-103.

Deutsch, J.A. (1971). The cholinergic synapse and the site of memory. Science, 174, 788-794.

Dews, P.B. and Wiesel, T.N. (1970). Consequence of monocular deprivation on visual behavior in kitten. Journal of Physiology, 206, 419-436.

Diamond, M.C., Krech, D. and Rosenzweig, M.R. (1964). The effects of an enriched environment on the histology of the rat cerebral cortex. Journal of Comparative Neurology, 123, 111-120.

Diamond, M.C., Law, F., Rhodes, H., Lindner, B., Rosenzweig, M.R., Krech, D. and Bennett, E.L. (1966). Increases in cortical depth and glia numbers in rats subjected to enriched environments. Journal of Comparative Neurology, 128, 117-126.

Diamond, M.C., Lindner, B and Raymond, A. (1967). Extensive cortical depth measurements and neuron size increases in the cortex of environmental enriched rats. Journal of Comparative Neurology, 131, 357-364.

Diamond, M.C., Johnson, R.E. and Ingham, C.A. (1975). Morphological changes in the young, adult and aging rat cerebral cortex, hippocampus and diencephalon. Behavioral Biology, 14, 163-174.

Diamond, M.C. (1976). Anatomical brain changes induced by environment. In: L. Petrinovich and J.L. McGaugh (Eds.), Knowing, thinking and believing (pp. 215-241). New York: Plenum Press.

Domjan, M., Schorr, R. and Best, M. (1977). Early environmental influences on conditioned and unconditioned ingestional and locomotor behavior. Developmental Psychobiology, 10, 499-506.

Donovick, P.J., Burright, R.G. and Swidler, M.A. (1973). Presurgical rearing environment alters exploration, fluid consumption and learning of septal lesioned and control rats. Physiology and Behavior, 11, 543-553.

Donovick, P., Burright, R. and Bengelloun, W. (1979). The septal region and behavior: an example of the importance of genetic and environmental factors in determining effects of brain damage. Neuroscience and Biobehavioral Reviews, 3, 83-96.

Doty, B.A. (1972). The effect of cage environment upon avoidance responding of aged rats. Journal of Gerontology, 27, 358-360.

Douglas, R.J. and Pribram, K.H. (1966). Learning and limbic lesions. Neuropsychologia, 4, 197-220.

Douglas, R.J. (1967). The hippocampus and behavior. Psychological Bulletin, 67, 416-442.

Douglas, R.J. and Pribram, K.H. (1969). Distraction and habituation in monkeys with limbic lesions. Journal of Comparative and Physiological Psychology, 69, 473-480.

Douglas, R.J. (1972). Pavlovian Conditioning and the Brain. In: R.A. Boakes and Halliday (Eds.), Inhibition and Learning (pp.529-553). New-York: Academic Press.

Eclander, F. and Karli, P. (1980). Effects of infant and adult amygdaloid lesions upon acquisition of two-way active avoidance by the adult rat: influence of rearing conditions. Physiology and Behavior, 24, 887-893.

Elnon, D., Morgan M.J. and Sahakian, B.J. (1975). The development of intersession habituation and emergence in socially reared and isolated rats. Developmental Psychobiology, 8, 553-559.

Einon, D.F. and Tye, M.C.(1975). Chlordiazipoxide and isolation induced timidity in rats. Psychopharmacologia, 44, 83-85.

Einon, D. and Morgan, M. (1976). Habituation of object contact in socially-reared and isolated rats. Animal Behaviour, 24, 415-420.

Einon, D.F. and Morgan, M.J. (1977). A critical period for social isolation in the rat. Developmental Psychobiology, 10, 123-132.

Einon, D.F. and Morgan, M.J. (1978). Early isolation produces enduring hyperactivity in the rat, but no effect upon spontaneous alternation. Quarterly Journal of Experimental Psychology, 30, 151-156.

Einon, D. (1980). Spatial memory and response strategies in rats: age, sex and rearing differences in performance. Quarterly Journal of Experimental Psychology, 32, 473-489.

Engellemer, W.J., Goodlett, C.R., Burright, R.G. and Donovick, P.J. (1982). Environmental enrichment and restriction: effects on reactivity, exploration and maze learning in mice with septal lesions. Physiology and Behavior, 29, 885-895.

Feigly, D.A., Parsons, P.J., Hamilton, L.W. and Spear, N.E. (1972). Development of habituation to novel environments in the rat. Journal of Comparative and Physiological Psychology, 79, 443-452.

Feldman, M.A. (1977). The effects of preexposure to a warning or a safety signal on the acquisition of a two-way avoidance response in rats. Animal Learning and Behavior 5, 21-24.

Ferchmin, P.A. and Bennett, E.L. (1975). Direct contact with enriched environments is required to alter cerebral weights in rats. Journal of Comparative and Physiological Psychology, 88, 360-367.

Ferchmin, P.A., Eterovic, V.A. and Levin, L.E. (1980). Genetic learning deficiency does not hinder environment-dependent brain growth. Physiology and Behavior, 24, 45-50.

Fessard, A. and Szabo, T. (1951). La facilitation de post-activation comme facteur de plasticite dans l'etablissement des liaisons temporaires. In: J.F. Delafresnaye (Ed.), Brain mechanisms and learning (pp.353-373). Oxford: Blackwell.

Fiala, B., Snow, F.M. and Greenough, W.T. (1977). "Impoverished" rats weigh more than "enriched" rats because they eat more. Developmental Psychobiology, 10, 537-541.

Fiala, B.A., Joyce, J.N. and Greenough, W.T. (1978). Environmental complexity modulates growth of granule cell dendrites in developing but not adult hippocampus of rats. Experimental Neurology, 59, 372-383.

Fifkova, E. (1970a). The effects of monocular deprivation on the synaptic contacts in the visual cortex. Journal of Neurobiology, 1, 285-294.

Fifkova, E. (1970b). Changes of axosomatic synapses in the visual cortex of monocularly deprived rats. Journal of Neurobiology, 2, 61-71.

Fifkova, E. (1970c). The effects of unilateral deprivation on visual centers in rats. Journal of Comparative Neurology, 140, 431-438.

Forgays, D.G. and Reid, J.M. (1962). Crucial periods for free-environmental experience in the rat. Journal of Comparative and Physiological Psychology, 55, 816-818.

Freeman, B.J. and Ray, O.S. (1972). Strain, sex and environment effects on appetitively and aversively motivated learning tasks. Developmental Psychobiology, 5, 101-109.

Gill, J.H., Reid, L.D. and Porter, P.B. (1966). Effects of restricted rearing on Lashley-stand performance. Psychological Reports, 19, 239-242.

Globus, A., Rosenzweig, M.R., Bennett, E.L. en Diamond, M.C. (1973). Effects of differential experience op dendritic spine counts in rat cerebral cortex. Journal of Comparative and Physiological Psychology, 82, 175-181.

Goodlett, C.R., Engellenner, W.J., Burricht, R.G. and Donovick, P.J. (1982). Influence of environmental rearing history and postsurgical environmental change on the septal rage syndrome in mice. Physiology and Behavior, 28, 1077-1081.

Grant, M. (1974). Cholinergic influences on habituation of exploratory activity in mice. Journal of Comparative and Physiological Psychology, 86, 853-857.

Greenough, W.T., Wood, W.E. and Madden, T.C. (1972). Possible memory storage differences among mice reared in environments varying in complexity. Behavioral Biology, 7, 717-722.

Greenough, W.T., Yuwiler, A. and Dollinger, M. (1973). Effects of posttrial eserine administration on learning in "enriched"- and "impoverished"- reared rats. Behavioral Biology, 8, 261-272.

Greenough, W.T. (1976). Enduring brain effects of differential experience and training. In: M.R. Rosenzweig and E.L. Bennett (Eds.), Neural mechanisms of learning and memory (pp. 255-278). Cambridge: The MIT Press.

Grouse, L.D., Schrier, B.K., Bennett, E.L., Rosenzweig, M.R. and Nelson, P.G. (1978). Sequence diversity studies of rat brain RNA: effects of environmental complexity on rat brain RNA diversity. Journal of Neurochemistry, 30, 191-203.

Gutwein, B.M. and Fishbein, W. (1980a). Paradoxical sleep and memory (I): Selective alterations following enriched and impoverished environmental rearing. Brain Research Bulletin, 5, 9-12.

Gutwein, B.M. and Fishbein, W. (1980b). Paradoxical sleep and memory (II): Sleep circadian rhythmicity following enriched and impoverished environmental rearing. Brain Research Bulletin, 5, 105-109.

Halgren, C.R. (1974). Latent inhibition in rats: associative or nonassociative? Journal of Comparative and Physiological Psychology, 86, 74-78.

Hall, G. and Minor, H. (1984). A search for context-stimulus associations in latent inhibition. Quarterly Journal of Experimental Psychology, 36B, 145-169.

Hall, G. and Channell, S. (1985). Differential effects of contextual change on latent inhibition and on the habituation of an orienting response. Journal of Experimental Psychology: Animal Behavior Processes, 11, 470-481.

Haracz, J.L. (1984). A neural plasticity hypothesis of schizophrenia. Neuroscience and Biobehavioral Reviews, 8, 55-71.

Hebb, D.O. (1949). The organization of behavior. New York: Wiley.

Held, J.M., Gordon, J. and Gentile, A.M. (1985). Environmental influences on locomotor recovery following cortical lesions in rats. Behavioral Neuroscience, 99, 678-690.

Horn, G., Rose, S.P.R. and Bateson, P.P.G. (1973). Experience and plasticity in the central nervous system. Science, 181, 506-514.

Hubel, D.H. and Wiesel, T.N. (1970). The period of susceptibility to the physiological effects of unilateral eye closure in kittens. Journal of Physiology (London), 206, 419-436.

Huntley, M.J. and Newton, J.M. (1972). Effects of environmental complexity and locomotor activity on brain weight in the rat. Physiology and Behavior, 8, 725-727.

Hyden, H. and Roennbaeck, L. (1978). Incorporation of amino acids into protein into different brain areas of rat, subjected to enriched and restricted environment. Journal of Neurological Science, 34, 415-421.

Hyden, H. and Roennbaeck, L. (1979). Proteins S-100 and 14-3-2 in nerve cells of rats raised in enriched and impoverished environments: Distribution, quantification, and cell separation by surface antigens. Behavioral and Neural Biology, 25, 371-379.

Jones, D.G. and Smith, B.J. (1980). The hippocampus and its response to differential environments. Progress in Neurobiology, 15, 19-69.

Joseph, R. and Gallagher, R.E. (1980). Gender and early environmental influences on activity, overresponsiveness, and exploration. Developmental Psychobiology, 13, 527-544.

Kiyono, S., Seo, M.L. and Shibagahi, M. (1981). Effects of rearing environments upon sleep-waking parameters in rats. Physiology and Behavior, 26, 391-395.

Konrad, K.W. and Bagshaw, M. (1970). Effect of novel stimuli on cats reared in a restricted environment. Journal of Comparative and Physiological Psychology, 70, 157-164.

Konrad, K and Melzack, R. (1975). Novelty-enhacement effects associated with early sensory-social isolation. In: A.H. Riesen (Ed.), Sensory deprivation (pp.253-276). New-York: Academic Press.

Krech, D., Rosenzweig, M.R., Bennett, E.L. and Krueckel, B. (1954). Enzyme concentrations in the brain and adjustive behavior patterns. Science, 120, 994-996.

Krech, D., Rosenzweig, M.R. and Bennett, E.L. (1956). Dimensions of discriminations and level of cholinesterase activity in the cerebral cortex of the rat. Journal of Comparative and Physiological Psychology, 49, 261-268.

Krech, D., Rosenzweig, M.R. and Bennett, F.L. (1960). Effects of environmental complexity and training on brain chemistry. Journal of Comparative and Physiological Psychology, 53, 509-519.

Krech, D., Rosenzweig, M.R. and Bennett, E.L. (1962). Relations between brain chemistry and problem solving among rats raised in enriched and impoverished environments. Journal of Comparative and Physiological Psychology, 55, 801-807.

Krech, D., Rosenzweig, M.R. and Bennett, E.L. (1963). Effects of complex environment and blindness on rat brain. Archives of Neurology, 8, 403-412.

Krechevsky, D. (1932a). "Hypotheses" versus "change" in the pre-solution period in sensory discrimination-learning. University California Publications of Psychology, 6, No 3.

Krechevsky, D. (1932b). "Hypotheses" in rats. Psychological Review, 39, 516-532.

Kuenzle, C.C. and Knusel, A. (1974). Mass training of rats in a superenriched environment. Physiology and Behavior, 13, 205-210.

La Torre, J.C. (1968). Effect of differential environmental enrichment on brain weight and on acetylcholinesterase and cholinesterase activities in mice. Experimental Neurology, 22, 493-503.

Leah, J., Allardyce, H. and Cummins, R. (1985). Evoked cortical potential correlates of rearing environment in rats. Biological Psychology, 20, 21-29.

Levin, P., Jand, J.K., Joseph, J.A., Ingram, D.K. and Roth, G.S. (1981). Dietary restriction retards the age associated loss of striatal dopaminergic receptors. Science, 561-562.

Levitsky, D.A. and Barnes, R.H. (1972). Nutritional and environmental interactions in the behavioral development of the rat: long-term effects. Science, 176, 68-71.

Lore, R.K. and Levowitz, A. (1966). Differential rearing and free versus forced exploration. Psychonomic Science, 5, 421-422.

Lore, R.K. (1969). Pain avoidance behavior of rats reared in restricted and enriched environments. Developmental Psychology, 1, 482-484.

Lovely, R.H., Pagano, R.R. and Paolino, R.M. (1972). Shuttle-box-avoidance performance and basal corticosterone levels as a function of duration of individual housing in rats. Journal of Comparative and Physiological Psychology, 81, 331-335.

Lovibond, P.F., Preston, G.C. and Mackintosh, N.J. (1984). Context specificity of conditioning, extinction, and latent inhibition. Journal of Experimental Psychology: Animal Behavior Processes, 10, 360-375.

Lubow, R.E. and Moore, A.U. (1959). Latent inhibition: the effects of non-reinforced pre-exposure to the conditioned stimulus. Journal of Comparative and Physiological Psychology, 52, 415-419.

Lubow, R.E. (1965). Latent inhibition: effects of frequency of non-reinforced pre-exposure to the CS. Journal of Comparative and Physiological Psychology, 60, 454-459.

Lubow, R.E. (1973). Latent inhibition. Psychological Bulletin, 79, 398-407.

Mackintosh, N.J. (1973). Stimulus selection: learning to ignore stimuli that predict no change in reinforcement. In: R.A. Hinde and J. Stevenson-Hinde (Eds.), Constraints on learning (pp. 75-100). London: Academic Press.

Mackintosh, N.J. (1975). A theory of attention: variations in the associability of stimuli with reinforcement. Psychological Review, 82, 276-298.

Manosevitz, M. and Joel, U. (1973) Behavioral effects of environmental enrichment in randomly bred mice. Journal of Comparative and Physiological Psychology, 85, 373-382.

Melzack, R. and Scott, T.H. (1957). The effects of early experience on the response to pain. Journal of Comparative and Physiological Psychology, 50, 155-161.

Melzack, R. (1969). The role of early experience in emotional arousal. Annals New York Ac. Science, 159, 721-730.

Meyers, B. (1971). Early experience and problem-solving behavior. In: H. Moltz (Ed.), The ontogeny of vertebral behavior (pp. 57-95). New York: Academic Press.

Mirmiran, M., Van den Dungen, H. and Uylings, H.B.M. (1982). Sleep patterns during rearing under different environmental conditions in juvenile rats. Brain Research, 233, 287-298.

Morgan, M.J. (1973). Effects of post-weaning environment on learning in the rat. Animal Behaviour, 21, 429-442.

Morgan, M.J., Einon, D.F. and Nicholas, D. (1975). Effects of isolation rearing on behavioral inhibition in the rat. Quarterly Journal of Experimental Psychology, 27, 615-634.

Morgan, M.J., Einon, D. and Morrison, R.G.M. (1977). Inhibition and isolation rearing in the rat: extinction and satiation. Physiology and Behavior, 18, 1-5.

Ough, B.R., Beatty, W.W. and Khalili, J. (1972). Effects of isolated and enriched rearing on response inhibition. Psychonomic Science, 27, 293-294.

Pribram, K.H., Douglas, R.J. and Pribram, B.J. (1969). The nature of nonlimbic learning. Journal of Comparative and Physiological Psychology, 69, 765-772.

Raaijmakers, W.G.M. (1978). Brain cholinesterase activity. Ph.D. Thesis, Nijmegen.

Ray, O.S. and Hochhauser, S. (1969). Growth hormone and environmental complexity effects on behavior in the rat. Developmental Psychology, 1, 311-317.

Reiss, S. and Wagner, A.R. (1972). CS habituation produces a "latent inhibition effect" but no active "conditioned inhibition". Learning and Motivation, 3, 237-245.

Rescorla, R.A. (1971). Summation and retardation tests of latent inhibition. Journal of Comparative and Physiological Psychology, 75, 77-81.

Riege, W.H. and Morimoto, H. (1970). Effects of chronic stress and differential environments upon brain weights and biogenic amine levels in rats. Journal of Comparative and Physiological Psychology, 71, 3, 396-404.

Riege, W.H. (1971). Environmental influences on brain and behavior of year-old rats. Developmental Psychobiology, 4, 157-167.

Rinaldi, P.C. and Thompson, R.F. (1985). Age, sex and strain comparison of habituation of the startle response in the rat. Physiology and Behavior, 35, 9-13.

Rosenzweig, M.R., Krech, D. and Bennett, E.L. (1960). A search for relations between brain chemistry and behavior. Psychological Bulletin, 57, 476-492.

Rosenzweig, M.R., Bennett, E.L. and Krech, D. (1964). Cerebral effects of environmental complexity and training among adult rats. Journal of Comparative and Physiological Psychology, 57, 438-439.

Rosenzeig, M.R. (1966). Environmental complexity, cerebral change, and behavior. American Psychologist, 21, 321-332.

Rosenzweig, M.R., Bennett, E.L. and Diamond, M.C. (1967). Transitory components of cerebral changes induced by experience. Proceedings, 75th Annual Convention, APA, 105-106.

Rosenzweig, M.R. and Bennett, E.L. (1968). Drugs modulate effects of environment on brain growth. Proceedings, 76th Annual Convention, APA, 269-270.

Rosenzweig, M.R., Love, W and Bennett, E.L. (1968). Effects of a few hours a day of enriched experience on brain chemistry and brain weights. Physiology and Behavior, 3, 819-825.

Rosenzweig, M.R. and Bennett, E.L. (1969). Brain weights and enzyme activities in gerbils, rats, and mice. Developmental Psychobiology, 2, 87-95.

Rosenzweig, M.R., Bennett, E.L., Diamond, M.C., Wu, S-Y., Slagle, R.W. and Saffran, E. (1969). Influences of environmental complexity and visual stimulation on development of occipital cortex in rat. Brain Research, 14, 427-445.

Rosenzweig, M.R. (1971). Effects of environment on development of brain and of behavior. In: E. Tobach, L.R. Aronson and E. Shaw (Eds.), The biopsychology of development (pp. 303-342). New York: Academic Press.

Rosenzweig, M.R. and Bennett, E.L. (1972). Cerebral changes in rats exposed individually to an enriched environment. Journal of Comparative and Physiological Psychology, 80, 304-313.

Rosenzweig, M.R., Bennett, E.L. and Diamond, M.C. (1972a). Cerebral effects of differential experience in hypophysectomized rats. Journal of Comparative and Physiological Psychology, 79, 56-66.

Rosenzweig, M.R., Bennett, E.L. and Diamond, M.C. (1972b). Chemical and anatomical plasticity of brain: Replications and extensions. In: J. Gaito (Ed.), Macromolecules and behavior, 2nd Ed. (pp. 205-277). New-York: Appleton-Century-Crofts.

Rosenzweig, M.R. and Bennett, E.L. (1976). Enriched environments: facts, factors, and fantasies. In: L. Petrinovitch and J.L. McGaugh (Eds.), Knowing, Thinking and Believing (pp. 179-213). New York: Plenum Press.

Rosenzweig, M.R. and Bennett, E.L. (1977). Effects of environmental enrichment of impoverishment on learning and on brain values in rodents. In: A. Oliverio (Ed.), Genetics, environment and intelligence (pp. 163-195). Amsterdam: Elsevier.

Rosenzweig, M.R. and Bennett, E.L. (1978). Experiental influences on brain anatomy and brain chemistry in rodents. In: G. Gottlieb (Ed.), Early Influences (Studies on the development of behavior and the nervous system, Vol. 4, pp. 289-327). New York: Academic Press.

Rosenzweig, M.R., Bennett, E.L., Hebert, M. and Morimoto, H. (1978). Social grouping cannot account for cerebral effects of enriched environments. Brain Research, 153, 563-576.

Ruiz-Marcos, A. and Valverde, F. (1969). The temporal evolution of the distribution of dendritic spines in the visual cortex of normal and dark raised mice. Experimental Brain Research, 8, 284-294.

Russell, P.A. and Williams, D.I. (1973). Effects of repeated testing on rats locomotor activity in the open-field. Animal Behaviour, 21, 109-112.

Sahakian, B.J., Robbins, T.W., Morgan, M.J. and Iversen, S.D. (1975). The effects of psychomotor stimulants on stereotypy and locomotor activity in socially-deprived and control rats. Brain Research, 84, 195-205.

Sahakian, B.J., Robbins, T.W. and Iversen, S.D. (1977). The effects of isolation rearing on exploration in the rat. Animal Learning and Behavior, 5, 193-198.

Schwartz, S. (1964). Effects of neonatal cortical lesions and early environmental factors on adult rat behavior. Journal of Comparative and Physiological Psychology, 57, 72-77.

Smith, H.V. (1972). Effects of environmental enrichment on open-field activity and Hebb-Williams problem solving in rats. Journal of Comparative and Physiological Psychology, 80, 163-168.

Solomon, P.R., Brennan, G. and Moore, J.W. (1974) Latent inhibition of the rabbit's nictating membrane response as a function of CS intensity. Bulletin of the Psychonomic Society, 4, 445-448.

Stein, D.G., Finger, S. and Hart, T. (1983). Pre and postoperational enrichment ("therapeutic") effects by brain lesions. Behavioral and Neural Biology, 37, 185-222.

Studelska, D.R. and Kimble, E.D. (1979). Effects of briefly experienced environmental complexity on open-field behavior in rats. Behavioral and Neural Biology, 26, 492-496.

Sturgeon, R.D. and Reid, L.D. (1971). Rearing variations and Hebb-Williams maze performance. Psychological Reports, 29, 571-580.

Sutherland, M. and Mackintosh, N.J. (1971). Mechanisms of animal discrimination learning. New-York: Academic Press.

Syme, L.A. (1973). Social isolation at weaning: some effects on two measures of activity. Animal Learning and Behavior, 1, 161-163.

Tagney, J. (1973). Sleep patterns related to rearing rats in enriched and impoverished environments. Brain Research, 53, 353-361.

Tryon, R.C. (1940). Genetic differences in maze learning ability in rats. Yearbook of the National Society Stud. Educ., 39, 111-119.

Uphouse, L. (1978). In vitro RNA synthesis by chromatin from three brain regions of differentially reared rats. Behavioral Biology, 22, 39-49.

Uphouse, L. and Moore, R.Y. (1978). Effect or rearing condition on in vitro RNA sythesis by brain chromatin. Behavioral Biology, 22, 23-38.

Uphouse, L. (1980). Reevaluation of mechanisms that mediate brain differences between enriched and impoverished animals. Psychological Bulletin, 88, 215-232.

Uylings, H., Kuipers, K., Diamond, M. and Veltman, W. (1978). Effects of differential environments on plasticity of dendrites of cortical pyramidal neurons in adult rats. Experimental Neurology, 62, 658-677.

Valverde, F. (1971). Rate and extent of recovery from dark rearing in the visual cortex of the mouse. Brain Research, 33, 1-11.

Van der Staak, C. (1976). Habituation and sensitization of the acoustic startle response during cortical spreading depression in rats. Physiology and Behavior, 16, 681-687.

Van der Staay, F.J. and Van Attekum-Hendriks, F.C. (1978). Anwendung eines klassisch mendelianschen kreuzungsschemas. Unpublished report, University of Nijmegen

Van Gool, W.A. and Mirmiran, M. (1984). Experience in an enriched environment alleviates active sleep reduction in old rats. Abstract to the 7th ESRS Congress, Munchen.

Vossen, J.M.H. (1966). Exploratief gedrag en leergedrag bij de rat. Amsterdam: Swets en Zeitlinger.

Vossen, J.M.H. (1968). Fysiologische psychologie en organiciteit. Nederlands Tijdschrift voor de Psychologie, 23, 69-95.

Vossen, J.M.H. (1973). Vergelijkend en fysiologisch-psychologisch onderzoek van leerprocessen. In: Ethologie, de biologie van gedrag (pp. 182-204). Wageningen: Centrum voor landbouwpublikaties en landbouwdocumentatie.

Wagner, A.R. and Rescorla, R.A. (1972). Inhibition in pavlovion conditioning: application of a theory. In: R.A. Boakes and M.S. Halliday (Eds.), Inhibition and learning (pp. 301-336). New-York: Academic Press.

Wagner, A.R. (1979). Habituation and memory. In: A. Dickinson and R.A. Boakes (Eds.), Mechanisms of learning and motivation. Hillsdale, New Jersey: Lawrence Erlbaum Association Inc..

Walsh, R.N., Budtz-Olsen, O.E., Penny, J.E. and Cummins, R.A. (1969). The effects of environmental complexity on the histology of the rat hippocampus. Journal of Comparative Neurology, 137, 261-266.

Walsh, R.N. and Cummins, R.A. (1975). Mechanisms mediating the production of environmentally induced brain changes. Psychological Bulletin, 82, 986-1000.

Walsh, R.N. and Cummins, R.A. (1979). Changes in hippocampal neuronal nuclei in response to environmental stimulation. International Journal of Neuroscience, 9, 209-212.

Walsh, R.N. (1980a). Effects of environmental complexity and deprivation on brain chemistry and Physiological: a review. International Journal of Neuroscience, 11, 77-89.

Walsh, R.N. (1980b). Towards an ecology of the brain. New York: Spectrum.

Walsh, R.N. (1981a). Effects of environmental complexity and deprivation on brain anatomy and histology: a review. International Journal of Neuroscience, 12, 33-51.

Walsh, R.N. (1981b). Sensory environments, brain damage, and drugs: a review of interactions and mediating mechanisms. International Journal of Neuroscience, 14, 129-137.

Warburton, D.M. and Groves, P.M. (1969). The effects of scopolamine on habituation of acoustic startle in rats. Comments in Behavioral Biology, 3, 289-293.

Warburton, D.M. and Brown, K. (1971). Attenuation of stimulus sensivity induced by scopolamine. Nature, 230, 126-127.

Warburton, D.M. (1972). The cholinergic control of internal inhibition. In: R.A. Boakes and M.S. Halliday (Eds.), Inhibition and Learning (pp. 431-460). New-York: Academic Press.

Warburton, D.M. (1977). Stimulus selection and behavioral inhibition. In: S.D. Iversen (Ed.), Drugs, neurotransmitters and behavior (Handbook of Psychofarmacology, Vol. 8, pp. 385-431). New York: Plenum Press.

Warburton, D.M. and Wesnes, K. (1984). Drugs as research tools in psychology: cholinergic drugs and information processing. Neuropsychobiology, 11, 121-132.

Warren, J.M., Zerweck, C. and Anthony, A. (1982). Effects of environmental enrichment on old mice. Developmental. Psychobiology, 15, 13-18.

Weiner, I., Schnabel, I., Lubow, R.E. and Feldon, J. (1985). The effects of early handling on latent inhibition in male and female rats. Developmental Psychobiology, 18, 291-297.

Weitzman, B. (1963). A threshold difference produced by a figure-ground dichotomy. Journal of Experimental Psychology, 66, 201-205.

Welker, W.I. (1957). "Free" versus "Forced" exploration of a novel situation by rats. Psychological Reports, 3, 95-108.

Whimbey, A.E. and Denenberg, V.H. (1967). Two independent dimensions in open-field performance. Journal of Comparative and Physiological Psychology, 63, 500-501.

Whishaw, I.Q., Zaborowski, J-A. and Kolb, B. (1984). Postsurgical enrichment aids adult hemidecorticated rats on a spatial navigation task. Behavioral and Neural Biology, 42, 183-190.

Will, B.E., Rosenzweig, M.R. and Bennett, E.L. (1976). Effects of differential environments on recovery from neonatal brain lesions, measured by problem-solving scores. Physiology and Behavior, 16, 603-611.

Will, B.E., Rosenzweig, M.R., Bennett, E.L., Hebert, M. and Morimoto, H. (1977). Relatively brief environmental enrichment aids recovery of learning capacity and alters brain measures after postweaning brain lesions in rats. Journal of Comparative and Physiological Psychology, 91, 33-50.

Williams, J.M., Hamilton, L.W. and Carlton, P.L. (1974). Pharmacological and anatomical dissociation of two types of habituation. Journal of Comparative and Physiological Psychology, 87, 724-732.

Woods, P.J., Ruckelhaus, S.I. and Bowling, D.M. (1960). Some effects of "free" and "restricted" environmental rearing conditions upon adult behavior in the rat. Psychological Reports, 6, 191-200.

Zimbardo, P.G. and Montgomery, K.C. (1957). Effects of 'free-environment" rearing upon explorative behavior. Psychological Reports, 3, 589-594.

Zolman, J.F. and Morimoto, H. (1965). Cerebral changes related to duration of environmental complexity and locomotor activity. Journal of Comparative and Physiological Psychology, 60, 382-387.

CURRICULUM VITAE

Gerard Joseph Marie van Woerden werd geboren op 8 september 1945 te Nijmegen. Hij bezocht de scholen Katwijk de Breul te Zeist en het Constantijncollege te Amersfoort, alwaar hij in juni 1964 het diploma H.B.S.-B behaalde. Na 1 jaar studie medicijnen, gevolgd door Militaire Dienst, begon hij in september 1967 met de studie psychologie. In juni 1970 werd het kandidaatsexamen afgelegd en in februari 1973 het doctoraal examen, met als hoofdvak vergelijkende en fysiologische psychologie, als uitbreidingen klinische psychologie en ontwikkelingspsychologie en als bijvak algemene neurofysiologie. Van 1 maart 1973 tot 1 mei 1976 was hij als wetenschappelijk medewerker werkzaam bij de vakgroep vergelijkende en fysiologische psychologie van de Universiteit Nijmegen, in het kader van een subsidie van de Nederlandse Vereniging voor Zuiver Wetenschappelijk Onderzoek (ZWO), middels de Nederlandse Stichting voor Psychonomie. Vervolgens was hij van 1 mei 1976 tot 1 september 1981 verbonden aan het verpleeghuis en de kliniek 'de Weerde' te Eindhoven. Vanaf 1 september 1981 is hij verbonden aan het St. Lambertus ziekenhuis te Helmond, welk ziekenhuis inmiddels per 1 januari 1986 gefuseerd is tot het Streekziekenhuis Gewest Helmond-Deurne.

STELLINGEN

1 Bij de uitvoering van dierexperimenteel onderzoek naar de werking van hersenen en gedrag vormt de kwaliteit van de voor-experimentele omgeving waarin de proefdieren zich bevinden een belangrijke variabele.

2 Het fenomeen 'latente inhibitie' is duidelijker waarneembaar bij ratten die zijn opgegroeid in een stimulusarme omgeving dan bij ratten die zijn opgegroeid in een stimulusrijke omgeving.

3 Bij onderzoek van leren geeft het onderzoek naar de manier en wijze waarop een proefdier een leerprobleem aanpakt en eventueel oplost vaak meer relevante informatie dan onderzoek naar de snelheid van - of het al dan niet in staat zijn tot - het oplossen van het probleem.

4 In het onderzoek naar cognitieve funktiestoornissen bij mensen met hersenbeschadiging geeft onderzoek naar de manier en wijze waarop de patient problemen aanpakt en eventueel oplost (via o.a. Luria's Neuropsychologische testmethodiek, gebaseerd op zijn theorie met betrekking tot het cognitief funktioneren en de relatie daarvan met het funktioneren van de hersenen) vaak veel meer relevante informatie dan onderzoek naar de snelheid van - of het al dan niet in staat zijn tot - het oplossen van het probleem (via bv. de meer klassieke 'organiciteits tests').

5 Bij de behandeling van mensen met hersenbeschadiging ten gevolge van een CVA, trauma en dergelijke dient cognitieve funktietraining een belangrijke plaats in te nemen.

6 Het onderzoek naar de kwaliteit van cognitieve funkties bij psychiatrische ziektebeelden dient krachtig gestimuleerd te worden.

7 Vroegtijdige inschakeling van psychologisch onderzoek en/of behandeling bij onbegrepen, chronische pijnklachten kan soms tot een grote kostenbesparing leiden, met name voor wat betreft medische verrichtingen.

8 De resultaten van onderzoek van Weiner en zijn medewerkers (1985) met betrekking tot de effekten van handling versus non-handling op het leren van mannelijke ratten, ondersteunen niet hun interpretatie dat handling een effekt heeft op het optreden van latent inhibition, maar wijzen wel op effekten op het aanleren van een two-way active avoidance response.

Weiner, I., Schnabel, I., Lubow, R.E. and Feldon, J. (1985). The effects of early handling on latent inhibition in male and female rats. Developmental Psychobiology, 18, 291-297.

9 De vragen 'is dit gedrag organisch' of 'zijn er aanwijzingen voor organiciteit' zijn triviaal. Beter is het deze vragen te formuleren als 'is deze afwijking beter somatisch dan wel psychologisch te behandelen'.

10 Het funktioneren van het menselijk brein is - metaforisch - op verschillende gebieden te vergelijken met dat van een symphonie-orkest: kan daar met het beperkt aantal instrumenten en tonen een schier eindeloze rij melodieën worden gecreeerd, zo ook geldt dat met het beperkt aantal onderdelen waaruit het brein bestaat (hippocampus, amygdala, schorsarealen etcetera) een schier eindeloze rij gedragingen kan worden gecreëerd.

11 De waarde van individuele autotests dient met de nodige scepsis bekeken te worden: de verschillen tussen meetgegevens van auto's van hetzelfde merk en type in diverse testonderzoeken, gepubliceerd in verschillende auto-bladen, zijn vaak groter dan de verschillen tussen de meetgegevens van auto's van vergelijkbare typen van verschillende merken, gepubliceerd in eenzelfde auto-blad, op grond waarvan vaak tot waarde-oordelen gekomen wordt.

12 De vreugde van wetenschappelijk onderzoek is niet gelegen in de ontdekking dat met iets weet, maar in de ontdekking dat men iets niet weet.

Nijmegen, 10 april 1986 G.J.M. van Woerden